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THE SEVENTY-SECOND ANNUAL CONVENTION (1924) OF THE AMERICAN PHARMACEUTICAL ASSOCIATION WILL BE HELD IN BUFFALO, N. Y.

The 1924 meetings of the American Conference of Pharmaceutical Faculties and the National Association of Boards of Pharmacy will also be held in Buffalo.

For Association Roster see pages x, xii, xiv, and xv.

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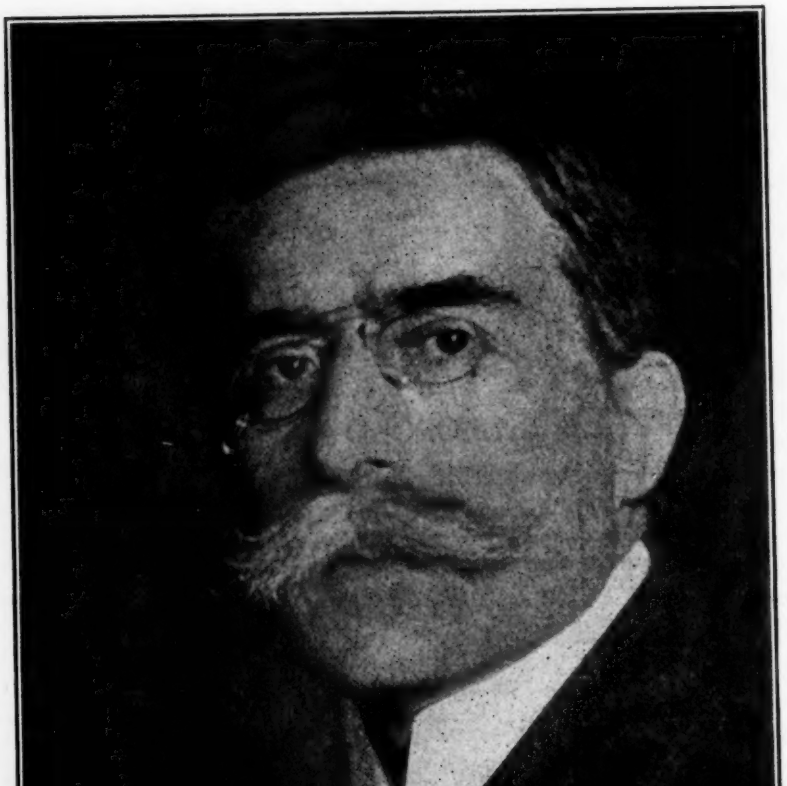


L. VAN ITALLIE

JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION

VOL. XII SEPTEMBER, 1923 No. 9

LEOPOLD VAN ITALLIE.

Leopold van Itallie was born March 12, 1866, in Maastricht, Holland. Here he obtained his preliminary education and in 1883 entered the University of Utrecht. In 1886 he was graduated as pharmacist and passed the State Board examinations. From 1886 to 1890 he was manager of a pharmacy in Harlingen; in the latter year he was appointed director and manager of the Community Pharmacy of Rotterdam, which position he held until 1902. During this period, he obtained leave of absence to study under Prof. Dr. Tschirch in Bern, Switzerland, and in 1901 he obtained his Ph.D. degree at the University of Bern. From 1902 to 1907 he was Professor at the Royal Veterinary School at Utrecht, his branches being Zoölogy and Pharmacology. From 1906 to 1907, he lectured on Pharmacognosy at the University of Utrecht, and since then he has served as Professor and Director of the Pharmaceutical Institute of the University of Leyden, Holland; the subjects under his direction here are Pharmaceutical Chemistry and Toxicology.

It is impossible in this brief sketch to enumerate the many papers read and published by Prof. van Itallie; over one hundred have appeared in the *Pharmaceutisch Weekblad*, in *Archiv der Pharmacie* and in the *Journal de Pharmacie et Chimie*. His chief research work has been in Phytochemistry and Toxicology. He is also author of several textbooks. From 1896 to 1907 he served as Editor of the *Pharmaceutisch Weekblad*. Since 1899 he has been a member of the Revision Committee of the Pharmacopœia of the Netherlands—from 1899 to 1910 as Secretary of the Committee and since 1910 he has been Chairman. He is a member of the Committee on the Codex on Food Standards of Holland, Chairman and Director of the Royal Institute for Pharmacotherapeutic Research, member of the National Food Commission, and of the Patent Bureau of Holland. During the year 1922–1923 he served as Rector of the University of Leyden. He is President of the International Pharmaceutical Federation and, in 1913, he served as Chairman of the 11th International Pharmaceutical Congress at the Hague, and was presiding officer of the recent Congress in London.

In addition to being an honorary member of the American Pharmaceutical Association Dr. Itallie holds honorary membership in many other pharmaceutical associations and other scientific organizations.

HUGO H. SCHAEFER.

EDITORIAL

E. G. EBERLE, Editor 253 Bourse Bldg., PHILADELPHIA

THE SEVENTY-FIRST ANNUAL MEETING OF THE AMERICAN PHARMACEUTICAL ASSOCIATION.

WHILE the transactions of the Seventy-first Annual Meeting of the American Pharmaceutical Association have become part of the history of the organization, a report thereon must be deferred till the next number of the JOURNAL—the convention week in Asheville being also the fixed time in the publication office for the completion of the September issue.

It may reasonably be assumed that the subject of greatest general interest for those assembled in Asheville during the week of September 3rd, and for American pharmacy, was the reorganization plan approved at the Cleveland A. Ph. A. meeting and presented during the year before State Pharmaceutical Associations in a way that resulted in endorsements by these units which, by the provisions of the plan, will be brought into closer relation with the parent organization. This is a first step toward a more comprehensive body pharmaceutic and association of organized groups representing the drug industries in its various activities and relations.

These lines, as indicated, were written prior to the opening date of the convention; deductions could be made from the recommendations by the State Pharmaceutical Associations, but our desire to draw conclusions, however reasonable the assumptions may be, is curbed by the realization that the plan to be activated is of momentous importance and the transactions of the Asheville meeting mark an epoch in the history of the American Pharmaceutical Association and American pharmacy. Also what in some respects would of necessity be a very incomplete survey at this writing will be general and authentic information at the time when this JOURNAL reaches the members. The possibilities of the plan are largely dependent on the morale of druggists and pharmacists, applying a meaning to the word as given by Herman J. Stich: "Morale is born of confidence—the confidence created by faith and determination, by enthusiasm and unflagging energy."

AN INTERNATIONAL PHARMACOPŒIA AND PHARMACEUTICAL NOMENCLATURE.

A MEETING of the International Pharmaceutical Federation was held in London during the week of July 23rd. The most important subject discussed during the convention related to the possibilities of preparing for an international pharmacopœia, which problem, as President van Itallie of the Federation said, lacks the merit of being a new one; preceding international congresses have discussed the same subject and the Federation Internationale Pharmaceutique was organized with such purpose in view.

The standard proposed by Prof. van Itallie restricts the number of items to be given recognition, but in general outline conforms to that followed in the revision of modern pharmacopœias—not only including potent medicines and brief descriptions, but in all cases giving methods of testing and, where necessary, those to be followed in preparing galenicals, etc. An international pharmacopœia conforming

to the viewpoints of Dr. van Itallie would provide standards for potent medicines and other materia medica that have been given official standing in the greater number of national pharmacopœias. The International Protocol needs correction and extension requiring international coöperation; unless that is made possible the work commenced at Brussels in 1902 will become less and less useful.

National pharmacopœias will not be replaced but international coöperation in their revision may prove advantageous, and an international guide has a value that deserves careful investigation. The Commission on Pharmaceutical Nomenclature of the International Pharmaceutical Federation has made progress and supports the foregoing statement; their report demonstrates the necessity for unification of titles and to that extent testifies in favor of an international standard.

In the preparation of the latter report sixteen pharmacopœias have been studied: Great Britain and United States (Anglo-American type); Belgium, France, Spain and Italy (French type); Denmark, Finland, Norway, Holland, Sweden (Northern type); Germany, Austria, Hungary, Russia and Switzerland (German type). A purpose is to select titles which will be acceptable as official designations in all pharmacopœias, and another is to aid in bringing about uniformity in preparations, as far as possible, so that the official title will be indicative of strength and purity.

The medicaments of the pharmacopœias named have been divided into three groups by the Commission:

A.—Chemical medicaments possessing a definite formula.

B.—Drugs of vegetable or animal origin.

C.—Compounded medicaments—galenicals, etc.

Of the first two classes all have been listed, but the latter (C) is incomplete because of wide variation in strengths, somewhat different composition of preparations but possessing about the same therapeutic properties, etc. The Latin title is followed by its corresponding appellation in Esperanto; an example of one official of each class is given for illustration:

Acidum arsenicosum = *Anhidrido arsenita; Arseniko.*
Ac. arsenicosum: AUS—DAN—FIN—GER—HEL.—HUN—NED—NOR—RUS—SV—FR—BEL.
Anhydridum arsenicosum: BEL—IT.
— arsenicosum: HIS—BRI.
Acidum arsenicosum: HIS.
Arseni trioxidum: U. S.

Adeps lanæ cum aqua = *Lanolino kun akvo.*
Adeps lanæ cum aqua: BEL—DAN—FR—HEL.—NED—NOR—RUS.
— — hydrosus: AUS—BR—HUN—U. S.
Lanolinum cum aqua: BEL—IT.
Lanolinum: GER—HEL.—HUN—NED—SV.
— hydricum: RUS.
Unguentum adipis lanæ: FIN.

Jalapa = *Jalapo.*
Exogonium Purga—Ipomœa Purga.
Jalapa: BRI—FIN—U. S.
Jalapæ radix: HUN.
— radicis tubera: IT.
Jalappæ tubera: BEL.
Radix jalappæ: AUS—HIS—NED.
Tuber jalapæ: AUS—DAN—FIN—GER—HEL.—NOR—RUS—SV.
Resina jalapæ: AUS—DAN—FR—NED—NOR—SV—U. S.

The British Pharmaceutical Conference and British Pharmaceutical Society were hosts on the occasion of the meeting of the Federation, and the delegates to the latter participated in the discussion of papers; those of one day of the convention were of an international type relating to international standards of drugs, uniformity in pharmaceutical preparations, etc.

In one of the closing addresses of the convention President van Itallie said:

"Our Federation is still in its infancy, and, indeed, its growth ceased entirely during the war. This meeting is proof of its resurrection and, I sincerely trust, of its rebirth to a new and vigorous life of useful activity. Our organization is not yet completed, and it is my hope that in the future our meetings will contribute materially to the advancement of pharmacy." E. G. E.

THE ABSORPTION OF DRUGS.

DOCTOR Cary Eggleston, as chairman of the Section on Pharmacology and Therapeutics, American Medical Association, delivered an address* on the subject indicated by the title, which is deserving of careful reading and study by pharmacists. Although the message was prepared for medical practitioners and intended to arouse a more general interest in the manifold problems of the absorption of drugs on the part of pharmacologists and clinicians, there is much in the address that will interest pharmacists. The presentation of facts bearing on absorption of drugs suggests opportunities for further investigations and some of the problems, in part at least, will appeal to the inquiring laboratory workers in the research departments of pharmacy schools.

Dr. Eggleston points out that the relation between the solubility of a drug in water and its absorbability is by no means so simple as is implied by the common statement that, since a particular modification of a drug is soluble, it is more readily absorbed than another which is relatively less soluble. He calls specific attention to the fact that the fluid in the digestive tract is not water, but is a complex solution of varying composition, capable of reacting with many drugs to render them soluble.

Continuing the discussion he refers to the absorption of alkaloids as hydrochlorides, irrespective of the form in which they are administered. He cites the salts of quinine and the alkaloid; although of varying solubility in water, the rate of absorption after administration is about the same. More striking, perhaps, are the results with quinidine alkaloid and the salts; comparative studies of absorption have shown that the differences in time of absorption bear no necessary relation to the question of solubility. Dr. Eggleston then comments that "it would be interesting to know the relative rates of absorption of these four compounds (those of quinidine) in patients with total achlorhydria and in normal persons, when introduced into the lower duodenum through a tube." He also points out the fact that ouabain is readily soluble, yet it is very poorly absorbed from the digestive tract, while digitoxin, which is almost insoluble, is readily absorbed. The influence of foods and of disease on absorption is also discussed in the paper.

Doctor Eggleston concludes the address deploring the tremendous lack of precise knowledge relative to the absorption of drugs, a knowledge of which seems very essential, and expresses the hope that the desire to investigate some of the problems in connection therewith will lead to a solution of them.

There seem also to be problems relative to the absorption of drugs with which the pharmacist is concerned. The dose of a drug is of necessity variable—it is defined by the author as "that amount which will just produce the desired effect in a given patient under the particular existing conditions." The relation between the rate of elimination and the duration of the action of a drug is another problem suggested by the paper for further investigation. E. G. E.

* San Francisco A. M. A. meeting. See *Journal A. M. A.*, August 11, 1923, p. 431.

ON 3-AMINO-4-HYDROXYARSENOPHENYL-4'-GLYCINE AND ITS *N*-METHYLENESULPHINATE AND *N*-METHYLENESULPHONATE DERIVATIVES.*

BY MERRILL C. HART AND WILBUR B. PAYNE.

The chemotherapeutic theory of Ehrlich, which is based on Witt's theory of dyeing, lays stress upon the importance of so-called anchoring groups, which causes the drug to selectively attach itself to certain cells or organisms. Upon the organism to which the drug is thus selectively attached the arseno group (pharmacophore) then exerts an efficient therapeutic activity.

As his work progressed, it became evident that the activity of arseno compounds was due not to specificity but to the formation within the body of oxidation products which had very marked trypanocidal activity. It could be demonstrated *in vitro* that arsenoxides exert this therapeutic effect at great dilutions. These substances are, however, toxic to the host. The arsonic acids are of little therapeutic value and likewise they are correspondingly not so toxic.

The important work of Voegtlin and his associates has demonstrated the mechanism by reason of which arseno compounds combine lowered toxicity to the host and trypanocidal action on the infection. Arseno compounds *per se* are slightly toxic, but in the blood stream they are oxidized through the arsenoxide (trivalent stage) to the arsonic acid (pentavalent) stage and excreted. An arseno compound, to be of value, must not explosively oxidize and afford a concentration of arsenoxide which will prove toxic to the host, nor yet must it oxidize so slowly that the concentration of arsenoxide never becomes effectively trypanocidal. The dosage used must be based on these considerations. Also the rate of excretion of both original drug and its alteration products while the above is taking place has an important bearing. As a guide in this problem, it is possible to determine experimentally the maximum tolerated dose and the minimum effective dose, and a drug which can be borne in large doses and which is oxidized to a sufficient concentration of arsenoxide to be effective in small doses ought to prove valuable.

One can readily see how far this is removed from Ehrlich's pioneer chemophore conception. It was his opinion that the arsphenamine molecule, with ortho amino phenol groups, possessed this specific property to the highest degree. If this is true Voegtlin would ascribe the specific properties, not to the groups, but to the physical properties with which these groups had endowed the molecule in which they are present.

This particular molecule will have certain solubilities, rates of diffusion, etc. These in turn will markedly influence the rate of oxidation, path of excretion, and tendency to deposition in various parts of the body. Thus in a very indirect manner is the chemotherapeutic effect attained.

The determination of the minimum effective dose experimentally is interesting and no doubt has great significance as to the clearing up of primary lesions, but these experimental infections are different from clinical syphilis. Any sample of neoarsphenamine will clear up the primary lesions, but of the picture beyond this we have nothing but clinical trial to rely on. It may well be that certain arseno

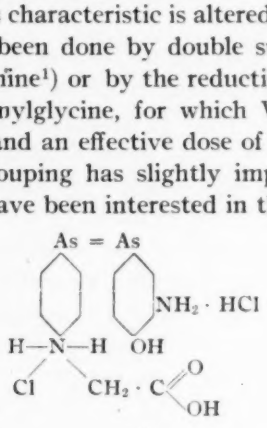
* Received for publication June 19, 1923.

compounds which respond poorly to the experimental requirements as to minimum effective does may prove valuable.

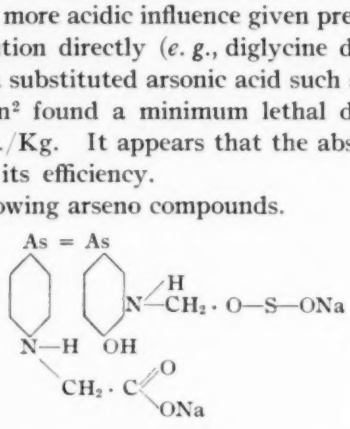
A large number of arseno derivatives have, of course, been prepared. Many of them have not been thoroughly studied. The description in the literature frequently betrays the fact that they have not been analyzed or prepared in such a manner as to warrant physiological study. Thus, 3-amino-4-hydroxyarsenophenyl-4′-glycine is described as red and must have been highly oxidized.

In arsphenamine the influence of the amino group is predominant. It has been a matter of great interest to observe the properties of arseno compounds in which this characteristic is altered and a more acidic influence given predominance. This has been done by double substitution directly (*e. g.*, diglycine derivative of arsphenamine[1]) or by the reduction of a substituted arsonic acid such as Ehrlich's arsenophenylglycine, for which Voegtlin[2] found a minimum lethal dose of 160 mg./Kg. and an effective dose of 10 mg./Kg. It appears that the absence of the phenol grouping has slightly impaired its efficiency.

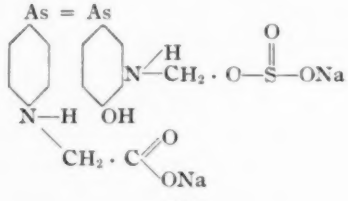
We have been interested in the following arseno compounds.



I.



II.



III.

If we consider (I) to be analogous to arsphenamine, (II) and (III) are comparable to neoarsphenamine and sulpharsphenamine, respectively.

The 3-amino-4-hydroxyarsenophenyl-4′-glycine (I) represents a compound that is very interesting from the theoretical standpoint to compare directly with arsphenamine. One-half of the molecule is identical with arsphenamine and the other half is deficient in the anchoring groups considered by Ehrlich to be necessary for the highest type of therapeutic efficiency and also contains the solubilizing group CH_2COOH. According to the theory of Ehrlich this compound would be decidedly inferior to arsphenamine therapeutically. If we consider the theory of Voegtlin that these groups merely act to modify the physical properties of the compound and these in turn influence the toxicity and the parasiticidal actively it is possible to conceive that this type of compound might be just as effective as arsphenamine. The laboratory findings tended to show that this compound was just as active therapeutically as arsphenamine and that the effect of the solubilizing

[1] D. R. P. 250,745.

[2] *J. Pharmacolog.*, 16, 6, 449, 1921.

group CH_2COOH was to lower the toxicity slightly and this was paralleled by a corresponding decrease in activity, the therapeutic ratio indicating this compound to be in the same class as arsphenamine.

At the present time more interest appears in the preparation of water-soluble condensation products which will prove somewhat less bothersome to handle. All these, however, appear to alter the arseno compounds in a similar manner, the characteristic increased solubility being the chief influence. As we go from arsphenamine to neoarsphenamine and sulpharsphenamine we produce compounds with a lower toxicity, but this decrease in toxicity is also accompanied by a corresponding decrease in their activity trypanocidally. We were interested in the question whether the introduction of these same groups would have the same effect in decreasing toxicity and trypanocidal activity when introduced in a molecule differing from arsphenamine in that it already had a solubilizing group (CH_2COOH) on one-half of the molecule, the other half being identical with arsphenamine (Compounds II and III).

These substances are readily prepared, and afford by comparison a measure for observing the influence of mono- and di-substitution by various groups on the same basic arseno compound. We were particularly interested in the different effects produced by substitution with the sulphur esters as distinct from the glycine substitutions. These results will be found in the summary.

The compound (I) 3-amino-4-hydroxyarsenophenyl-4′-glycine can be prepared by two methods. The 3-amino-4-hydroxyphenyl arsine reacts[1] with 4-glycinephenyl arsenious oxide (or chloride) to form the desired product. A much simpler method for its production is the reduction[2] of equimolecular mixtures of phenylglycine-*p*-arsenious chloride hydrochloride and 3-amine-4-hydroxyphenylarsenious oxide with sodium hydrosulfite.

EXPERIMENTAL.

The Action of Chloroacetic Acid upon 3-Amino-4-hydroxyphenylarsinic Acid.—3-Amino-4-hydroxyphenylarsinic acid 2.33 Gm. (1 mol.), chloroacetic acid 1.89 Gm. (2 mols.), sodium carbonate 2.1 Gm. (2 mol.), and potassium iodide, 3.2 Gm. (2 mols.), were heated under a reflux for $1^1/_2$ hours. A further quantity of sodium carbonate (0.5 Gm.) was required to render the solution yellow to methyl red, and the heating was continued two hours longer. The solution (100 cc) concentrated to 25 cc and acidified with acetic acid yielded no precipitate. It was concentrated to 10 cc, acidified with hydrochloric acid and upon standing 0.75 Gm. material crystallized (m. p. 255°). It was recrystallized from 5 cc of hot water and analyzed after drying it at 130° in a vacuum.

Subs., 0.1111 Gm., 6.79 cc, 0.1 *N* $Na_2S_2O_3$ (Lehmann).
Subs., 0.1723, 0.0824 Gm. $Mg_2As_2O_7$.
Calc. for $C_{10}H_{10}O_7NAs$, As, 22.7. Found, As, 22.92, 23.08.

The substance is probably an anhydride of the diglycine with both acetic groups on the nitrogen.

3-Amino-4-hydroxyphenylarsinic Acid.—This compound was prepared from 3-nitro-4-hydroxyphenylarsinic acid by reduction with ferrous hydroxide.[3] This

[1] D. R. P. 254,187.
[2] D. R. P. 251,104.
[3] W. A. Jacobs and M. Heidelberger, *J. Am. Chem. Soc.*, 40, 1580, 1918.

was purified by dissolving it in the calculated quantity of normal sodium hydroxide, treating it with animal charcoal, filtering hot, and precipitating with acetic acid. By this means, the 3-amino-4-hydroxyphenylarsinic acid was obtained as a white crystalline compound entirely soluble in dilute hydrochloric acid. It was dried to constant weight *in vacuo* and analyzed.

Subs., 0.2500, 0.2500, 21.08, 21.08 cc, 0.1 *N* $Na_2S_2O_3$ (Lehmann).
Calc. for $C_6H_8O_4NAs$, As, 32.19. Found As, 31.60, 31.60.

3-Amino-4-hydroxyphenylarsenious Oxide.—This substance was prepared by the method of Ehrlich and Bertheim[1] by the reduction of 3-amino-4-hydroxyphenylarsinic acid by sulphur dioxide. By this method preparations containing 40 to 60 per cent. of the oxide mixed with salt were produced. These were analyzed for arsenic and also by titration with iodine. It was found that the titration with iodine tended to give slightly high results and the figure for arsenic was used in all the calculations.

Phenylglycine-p-arsinic Acid.—This was prepared by the method outlined by Morgan.[2] The crude product was washed with dilute hydrochloric acid and crystallized from hot water. From 100 grams of arsanilic acid, 94 grams of dry crystalline acid were obtained. This was entirely soluble in dilute sodium bicarbonate solution.

Phenylglycine-p-arsenious Chloride Hydrochloride.[3]—Forty grams of the phenylglycine-*p*-arsinic acid were dissolved in 200 cc of hydrochloric acid (sp. gr. 1.19) to which 1 Gm. of potassium iodide was added. This solution was cooled in salt ice-bath to —10° C. and saturated with sulphur dioxide. A crystalline magma formed which was filtered off and washed with acetic acid and then with ether. It was dried to constant weight *in vacuo* over sodium hydroxide. Yield, 32.2 Gm.

Subs., 0.2000, 11.61 cc, 0.1 *N* $Na_2S_2O_3$ (Lehmann).
Calc. for $C_8H_9O_2NAsCl_3$, As, 22.55. Found, 21.76.

3-Amino-4-hydroxyarsenophenyl-4′-glycine.—We attempted to prepare this compound by reduction with hydrosulphite of equimolecular mixtures of the two different arsinic acids. Varying conditions as to time, temperature and acidity were employed, but in all cases mixtures were obtained usually with arsphenamine predominating. It thus appears that this class of compounds are not necessarily produced by this process. A review of the patent literature indicates this fact, but, on the contrary, one gathers from the current literature that this is a method of general application.

When 3-amino-4-hydroxyarsenophenyl-4′-glycine is prepared in pure condition in such a manner to prevent oxidation from exposure to the air it forms a bright yellow amorphous substance which dissolves in dilute sodium bicarbonate solutions and in dilute hydrochloric acid. The corresponding dihydrochloride when prepared by the Ehrlich process tends to hydrolyze so that dilute aqueous solution may appear very slightly turbid. Such a solution (1–100) will clear up when a few drops of tenth-normal hydrochloric acid is added. Such a solution when gradually

[1] *Ber.*, 45, 1, 756, 1912.
[2] G. T. Morgan, "Organic Compounds of Arsenic and Antimony," p. 165.
[3] D. R. P. 251,104.

treated with dilute bicarbonate at first precipitates the free arseno compound which redissolves with more of the bicarbonate to a brilliantly clear solution. It can be precipitated with acetic acid. The presence of free carbonic acid tends to retard a second solution with bicarbonate, and the bicarbonate solution can be precipitated by saturation with carbon dioxide.

The solubility in dilute bicarbonate and hydrochloric acid is the best criterion for the purity of this compound, as the arsenic to nitrogen or arsenic to chlorine ratios signify nothing as to its purity.

In order to prepare this arseno compound in a condition of sufficient purity to satisfy the above-mentioned solubility requirements we proceeded as follows: 24.96 Gm. of phenylglycine-*p*-arsenious chloride hydrochloride and 14.94 Gm. (37.58 Gm. of 40% material) of 3-amino-4-hydroxyphenylarsenious oxide were dissolved in 120 cc of methyl alcohol. This solution was poured into 300 cc of normal sodium hydroxide in a reduction cell[1] and diluted with 1200 cc of water. To this 120 Gm. of pure sodium hydrosulphite are added. The reduction takes place almost immediately at room temperature with the production of a heavy light yellow precipitate. The reaction was allowed to run for 15 minutes. At the end of this time, the base was filtered off, washed and dried and the hydrochloride prepared and ampouled using similar apparatus and technique to prevent oxidation used by Heyl and Miller for the preparation of pure arsphenamine hydrochloride. Seventy-five cc of 2 *N* methyl alcoholic hydrochloric acid diluted to 225 cc with absolute methyl alcohol were used for the solution of the base. For the precipitation of the hydrochloride, 2 liters of dry ether were sufficient. This gave 26 Gm. (72% theory) of the dihydrochloride. It was an amorphous light yellow powder.

Due to the colloidal nature of this material, the base filtered and dried very slowly even at pressures of 2–3 mm. of mercury. For the preparation of smaller amounts of this substance, it was found more convenient to centrifuge the base, wash it thrice with water, twice with absolute alcohol and once with ether. Because of the slight solubility of the base in alcohol, the yields (60–65% theory) by this method were not as good as the method given above.

One preparation was dried to constant weight *in vacuo* at 75° C. and analyzed. Volatile matter = 7.04%.

Analyses: Subs., 0.2000, 0.2000: 16.38, 16.48 cc, 0.1 *N* $Na_2S_2O_3$ (Lehmann).
Subs., 0.2325, AgCl, 0.1480.
Calc. for $C_{14}H_{14}O_3N_2As_2.2HCl$, As, 31.18; Cl, 14.76. Found, As, 30.69, 30.88, Cl, 15.74.

This material contained small amounts of sulphur.

Analysis: Subs. 0.3605, $BaSO_4$, 0.0075. Found, S, 0.28%.

Toxicity by the Rat Method.—3-Amino-4-hydroxyarsenophenyl-4′-glycine is less toxic than the arsphenamine. This property falls midway between arsphenamine and the well-known neoarsphenamine. The substance presents marked colloidal properties, and is somewhat more difficultly soluble than arsphenamine. For injection two per cent. solutions were employed. The substance was first dissolved in fresh distilled water and then made alkaline with the calculated quantity of nor-

[1] Heyl and Miller, JOUR. A. PH. A., 11, 434, 1922.

mal sodium hydroxide (4 moles) and made up to the mark. The observational period was 48 hours.

TABLE I.

TOXICITY OF SODIUM-3-AMINO-4-HYDROXYARSENOPHENYL-4′-GLYCINE.

			Doses in mg./Kg.									
Expt.	As, %.	Cl, %.	150.		175.		200.		225.		250.	
54	28.54	14.64	+ + + + +		— — — — —							
60	29.68	13.03	+ + + + —		+ + — — —		+ + — — —					
65	27.78	14.93			+ — — — —		+ + + + —					
65	27.78	14.93	— — + + +		+ + + + +		+ + + + +		— — — — —		— — —	
87	29.52	15.36	+ + + + —		+ + + — —							

+ Lived. — Died.

The maximum tolerated dose ranged from 150 to 200 mg./Kg. 78% of the deaths took place within the first 24 hours. It is well known that the toxicity of an arsphenamine solution can be decreased by standing, etc. 3-Amino-4-hydroxyarsenophenyl-4′-glycine shows this property to such an extent that we have observed animals injected with smaller doses to succumb, while injections made later proved less toxic. In Expt. 65 above, this is well illustrated.

Trypanocidal Activity of Sodium-3-amino-4-hydroxyarsenophenyl-4′-glycine.—Some observations were made to determine the minimum effective dose required to sterilize rats which had previously been infected with *Trypanosoma equiperdum.*[1] The methods employed by Voegtlin and Miller[2] were used. The therapeutic ratio (m. l. d./m. e. d.) was determined on two samples having a minimum lethal dose of 175 mg./Kg. The experimental infection was fairly uniform and varied from 150,000 to 250,000 per cmm. of blood. In order to sterilize in 24 hours, 5.2 to 9.2 mg./Kg. were necessary. If the observations as to sterility were made in 21 days the average dose required was 11.8 mg./Kg. For the 24-hour period the therapeutic ratio is from 19 to 33 and for the 21-day period, 15. Voegtlin and Miller found the therapeutic ratio of arsphenamine to vary between 13.2 and 26 and for neoarsphenamine it averaged 24.3 so that the safety of this drug is of the same order.[3]

Sodium-3-amino-4-hydroxyarsenophenyl-4′-glycine-N-methylenesulphinate.—We were interested in blocking both of the amino groups and to observe the effect of this on the toxicity and the parasiticidal activity of the drug. 3-Amino-4-hydroxyarsenophenyl-4′-glycine was therefore condensed with sodium formaldehyde sulphoxylate using the apparatus to prevent oxidation described by Heyl and Miller,[4] for the preparation of pure neoarsphenamine.

The glycine derivative (8 Gm.) was dissolved in 50 cc of absolute methyl alcohol. Nine cc of 50% formaldehyde sulphoxylate were used and the reaction ran for 3 minutes at 21° C. At the end of this time 12 cc of water and 23.5 cc of 10% sodium carbonate solution were added. The filtered solution was precipitated by running it into 400 cc of absolute alcohol. Made by this procedure the sodium 3-amino-

[1] The strain of *Trypanosoma equiperdum* used in this work was kindly furnished by Dr. Dyer of the Hygienic Laboratory, U. S. P. H. S.

[2] *Public Health Reports*, 37, 27, 1627, 1922.

[3] Clinical study of 3-amino-4-hydroxyarsenophenyl-4′-glycinedihydrochloride has been undertaken by Dr. A. D. Hirschfelder of the Pharmacology Department, University of Minnesota.

[4] *Loc. cit.*

4-hydroxyarsenophenyl-4′-glycine-*N*-methylenesulphinate formed a bright yellow, extremely soluble amorphous powder. It was dried in the usual way *in vacuo* over P_2O_5 and ampouled. 80% yields were obtained by this method. The dried powder averaged 25.66% arsenic content.

Determination of the Maximum Tolerated Dose.—For the determination of this value we used the same procedure given by us[1] for the determination of the maximum tolerated dose of neoarsphenamine. 3.088 Gm. of the hydrochloride of 3-amino-4-hydroxyarsenophenyl-4′-glycine (As, 28.5%) were dissolved in 15 cc of methyl alcohol. The condensation was made with 3.60 cc of 50% formaldehyde sulphoxylate solution (2 mols.). The reaction was complete in 3 minutes at 21° C. The yellow precipitated neo-compound is dissolved in 9.34 cc of 10% sodium carbonate forming the di-sodium salt. The solution after the removal of the alcohol in a vacuum is made up quantitatively to 110 cc. This solution represents 4% solution of the drug containing 20% arsenic. This arsenic content was selected to make the results directly comparable with neoarsphenamine.

Sodium 3-amino-hydroxyarsenophenyl-4′-glycine-*N*-methylene sulphinate is a more delicate chemical than neoarsphenamine. When the time of reaction is increased and the temperature of the condensation raised to 29° C. discoloration of the solution and increased toxicity result. (See Expt. 67, Table II.)

TABLE II.

TOXICITY OF SODIUM-3-AMINO-4-HYDROXYARSENOPHENYL-4′-GLYCINE-*N*-METHYLENESULPHINATE.

Expt.	"Glycine" used.	Temp.	Time.	As, %.	Doses in mg./Kg. 250.	300.	350.	400.	450.
67	54	29°	15 min.	20.3	+++++	++−−−		−−−−−	
73	60	25°	5 min.	20.33	+++++	+++++−	+++++−		
83	60	21°	3 min.	19.72			+++++	+++−−	−−−−−
85	65	21°	3 min.	18.98			+++++	+++−−	−−−−−

\+ Lived. − Died.

The rats used for the above tests showed a tolerance of 480 mg./Kg. for neoarsphenamine (20% arsenic). Similar to high test neoarsphenamine a majority of the deaths (86%) took place in the first 24 hours. This "neo-glycine" as far as toxicity is concerned is comparable to neoarsphenamine having a maximum tolerated dose of from 350 to 400 mg./Kg. (20% As).

Trypanocidal Activity of Sodium-3-amino-4-hydroxyarsenophenyl-4′-glycine-N-methylenesulphinate.—This was determined in a similar manner to that of the parent glycine derivative. The infection varied from 100,000 to 300,000 to the cmm. of blood. For sterilization in 24 hours dosages of 19 to 28 mg./Kg. were required. For the 21-day periods a 28 mg./Kg. dose was sufficient. The m.l.d. was 450 mg./Kg. at 20% arsenic. The therapeutic ratio found therefore varied from 16 to 24 for the 24-hour period and was 16 for the 21-day period.

These preparations were analyzed to observe the extent of the condensation. Twenty-five cc of the 4% solution were diluted to 60 cc with water and precipitated in the cold with 6 cc of normal hydrochloric acid. The slightly yellow precipitated "neo-acid" was centrifuged off and washed thrice with ice-cold water containing 2 cc of normal hydrochloric acid and then made up to 50 cc quantitatively with

[1] M. C. Hart and W. B. Payne, *J. Am. Chem. Soc.*, 44, 5, 1150, 1922.

water containing 4 cc of normal sodium hydroxide. Aliquots of this solution were used for the determination of arsenic, total sulphur, and sulphur condensed on the amino group ($NHCH_2OSOH$) using the same methods reported by us in a previous paper.[1] An average recovery of 98 per cent. of the arsenic in the precipitated and washed "neo-acid" showed the absence of any appreciable amount of the unchanged parent glycine in this product. The calculations are reported in terms of atomic ratios. Theory for the pure mono-methylenesulphinic acid derivative requires 2 arsenic to 1 sulphur. The findings are as follows:

TABLE III.

SULPHUR DISTRIBUTION IN 3-AMINO-4-HYDROXYARSENOPHENYL-4′-GLYCINE-*N*-METHYLENESULPHINATE.

Expt.	Temp.	Time.	Total S.	"Amino" S.	Nuclear S.
67	29° C.	15 min.	1.00	0.95	0.05
73	25° C.	5 min.	0.94	0.90	0.04
83	21° C.	3 min.	0.93	0.90	0.03
85	21° C.	3 min.	0.95	0.92	0.03

The reaction is practically complete in 3 minutes at 21° C. A higher temperature and a longer time (No. 67) gives a compound closer to the theoretical As to S ratio but darker in color and more toxic (see Table II).

Sodium-3-amino-4-hydroxyarsenophenyl-4′-glycine-N-methylenesulphonate.—It was thought that this derivative might have more satisfactory properties than the corresponding methylenesulphinate described above. Voegtlin and Smith[2] have described the di-methylenesulphonate of arsphenamine (sulpharsphenamine).

The introduction of the methylenesulphonate group in this case produces a compound that can be injected subcutaneously and which is quite stable when exposed in solution to the air.

The same precautions used in the preparation of all of these compounds to prevent oxidation from the air were also used in the preparation of this derivative. To 3-amino-4-hydroxyarsenophenyl-4′-glycine dihydrochloride 4 Gm. (27.8% As) dissolved in 6 cc of alcohol and 56 cc of water are added 0.66 cc of $33\frac{1}{3}\%$[3] formalin solution (1 mol.). After one minute 5.04 cc of 30% sodium hydrogen sulphite solution (2 mols.) were added. An immediate thick yellow precipitate was formed that slowly went into solution. At the end of 7 minutes 8 cc of 10% sodium carbonate solution were added. After 16 minutes it was filtered out of contact with air and precipitated by running it into 320 cc of absolute alcohol. The yellow granular precipitate was centrifuged off and washed twice with 150 cc of absolute alcohol. It was dried to constant weight *in vacuo* over sodium hydroxide and phosphoric anhydride. A yield of 4.08 Gm. was obtained. This was ampouled up and sealed in the presence of carbon dioxide in the usual manner. This compound formed a golden yellow amorphous powder averaging 23.8% arsenic. Solutions of it did not darken on exposure to the air in contradistinction to neoarsphenamine. Similar to Voegtlin and Smith's sulpharsphenamine this

[1] M. C. Hart and W. P. Payne, *Loc. cit.*

[2] Voegtlin and Smith, *J. Am. Chem. Soc.*, 44, 2574, 1922; also D. R. P. 249,726.

[3] The strength of the formalin and bisulphite solutions were determined by analysis.

compound did not reduce indigo carmine[1] solution showing the absence of the sulphinic acid grouping. Upon treating this with zinc and acetic acid the filtrate will reduce the indigo carmine solution due to the formation of the CH_2OSONa grouping.

One of these preparations was used for the preparation and analysis of the free acid. Two grams of the di-sodium salt of the 3-amino 4-hydroxyarsenophenyl-4′-glycine-*N*-methylenesulphonate were taken up in 8 cc of water and precipitated with 30 cc of glacial acetic acid. The yellow precipitated acid was centrifuged off and washed thrice with 25 cc of 80% acetic acid and finally dried to constant weight *in vacuo* over sodium hydroxide and finally over phosphoric anhydride. The yield of the dried acid was 1.250 grams. This was dried to constant weight *in vacuo* at 100° C. and analyzed. Moisture = 12.95%.

Analysis: Subs., 0.2000, 0.2000: 16.28, 16.38 cc 0.1 *N* $Na_2S_2O_3$ (Lehmann).
Subs., 0.3000, 0.3000, $BaSO_4$, 0.1329, 0.1348.
Calc. for $C_{15}H_{16}N_2O_6As_2S$: As, 29.88, S, 6.37. Found As, 30.50, 30.69, S, 6.08, 6.17.

The above figures for arsenic and sulphur when calculated in terms of atomic ratios indicate that the condensation had occurred to the extent of 94%.

Toxicity and Trypanocidal Activity of Sodium-3-amino-4-hydroxyarsenophenyl-4′-glycine-N-methylenesulphonate.—Two runs of this compound were prepared and the toxicity and trypanocidal activity determined. The minimum lethal dose in 4% solution (24% arsenic) by the official method for neoarsphenamine varied from 250 to 300 mg./Kg. The rats used for these tests showed a tolerance of 480 mg./Kg. for neoarsphenamine (20% arsenic). On rats carrying an infection of 100,000 to 180,000 of Trypanosoma equiperdum per cmm. of blood the dose required to sterilize for 24 hours as well as for the 3-day period was 15.5 mg./Kg. The therapeutic ratio therefore varied from 16 to 20.

Solutions of this compound could also be injected subcutaneously. By this method the minimum lethal dose was 350 mg./Kg. Subcutaneously it was also very active trypanocidally. 31 mg./Kg. doses were sufficient to sterilize rats for the 24-hour period which had an infection of 150,000 to 250,000 per cmm. of the trypanosomes. For the 3-day period doses of 23 mg./Kg. were required. The therapeutic ratio by this method is 11 to 15.

Solutions of this compound were quite stable when exposed to the air. A solution which killed 2 out of 5 rats at 250 mg./Kg. when allowed to stand 24 hours in an open cylinder exposed to air killed none out of 5 rats at the same dosage.

TABLE IV.

TOXICITY OF SODIUM-3-AMINO-4-HYDROXYARSENOPHENYL-4′-GLYCINE-*N*-METHYLENESULPHONATE.

		Doses in mg./Kg.			
Expt.	Injection.	200.	250.	300.	350.
89	Intraven.	+++++	++−−−		−−−
90	Intraven.	+++++	+++−−	−−−	−−−
90	Intraven.[1]	+++++	+++++	++++−	+−−−−
89	Subcut.	+++++	++++−	++++−	−−−
90	Subcut.			++++−	+−−−−

[1] Solution allowed to stand exposed to the air in an open cylinder for 24 hours.

[1] Reinking, Dehnel and Labhardt, *Ber.*, 38, 1069, 1905.

At a dose of 300 mg./Kg. one out of 5 rats were killed showing an actual decrease in toxicity on standing.

SUMMARY.

1. The following unsymmetrical arseno compounds have been prepared and studied with the following results:

(*a*) 3-Amino-4-hydroxyarsenophenyl-4′-glycine for which the maximum tolerated dose was found to be 150 to 200 mg./Kg. with a therapeutic index of 19 to 33 for the 24-hour period and 15 for the 21-day period.

(*b*) 3 - Amino - 4 - hydroxyarsenophenyl - 4′ - glycine - *N* - methylenesulphinate for which the maximum tolerated dose was found to be 350 to 400 mg./Kg. (20% As) and the therapeutic index 16 to 24 for the 24-hour period, and 16 for the 21-day period.

(*c*) 3 - Amino - 4 - hydroxyarsenophenyl - 4′ - glycine - *N* - methylenesulphonate for which the minimum lethal dose (intravenously) was 250 to 300 mg./Kg. and subcutaneously was 350 mg./Kg. (24% As). The therapeutic ratio of this intravenously varied from 16 to 20 for both the 24-hour and the 3-day period and subcutaneously it was 11 for the 24-hour period and 15 for the 3-day period. This compound is also very stable in solution and becomes less toxic on standing exposed to the air for 24 hours.

2. The introduction of the methylenesulphinate group into 3-amino-4-hydroxyarsenophenyl-4′-glycine reduces considerably the toxicity of the compound. The activity of the compound trypanocidally is also correspondingly reduced. The advantage in the introduction of this group into the molecule in this case is the production of a water-soluble derivative that is easier to handle clinically.

3. The introduction of the methylenesulphonate group into the molecule of the 3-amino-4-hydroxyarsenophenyl-4′-glycine results in a slighter diminution of the toxicity than the methylenesulphinate group. However, the activity is correspondingly slightly reduced. The great advantage though in the introduction of this group is the production of a water-soluble derivative that is stable when exposed to the air and which also can be injected subcutaneously.

4. The effect of the introduction of the methylenesulphinate and the methylenesulphonate group into the 3-amino-4-hydroxyarsenophenyl-4′-glycine on therapeutic activity (m. l. d./m. e. d.) parallels the effect of the same groups when introduced into arsphenamine.

5. The series of compounds described above are deficient in some of the essential anchoring groups considered by Ehrlich to be necessary for the highest type of therapeutic efficient which he claims to have reached in arsphenamine. If this is true these compounds should be distinctly inferior to the corresponding ones in the arsphenamine series (arsphenamine, neoarsphenamine, and sulpharsphenamine). The laboratory tests, however, did not substantiate the theory of Ehrlich but showed that these compounds were just as effective, therapeutically, as the corresponding ones in the arsphenamine series.

In conclusion we wish to thank Dr. Frederick W. Heyl at whose suggestion this work was carried out.

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REVIEW OF METHODS OF ASSAYING OIL OF BITTER ALMOND.

BY JANE L. HASTINGS.

True oil of bitter almond is obtained from the seeds of *Prunus Amygdalus amara* DeCandolle, after the fixed oil has been removed by expression. However, the essential oils from the kernels of apricots and peaches are identical for all practical purposes with the true almond oil. In fact, most of the so-called bitter almond oil of commerce is derived from apricots. The essential oil, as we know it, is not present in the kernels as such. It is formed by the action—in the presence of water—of emulsin, a natural ferment, on amygdalin, both being natural constituents of the seeds. By the reaction, benzaldehyde, dextrose and hydrocyanic acid are formed. The following equation expresses the reaction:

$$C_{20}H_{27}O_{11}N + 2H_2O = 2C_6H_{12}O_6 + C_6H_5.CHO + HCN$$

Amygdalin is a crystalline glucoside which has no odor of bitter almond and is not converted to the oil except by a hydrolytic agent, either water or by boiling with dilute acids.

The pure oil consists almost wholly of benzaldehyde. On account of this there has been a great deal of adulteration of the oil with artificial benzaldehyde. Benzaldehyde oxidizes to benzoic acid if allowed to stand in the air. Therefore it is necessary that bottles of the oil should be kept well stoppered and as full as possible. Schimmel & Company state that the addition of 10 per cent. of alcohol retards oxidation and alcohol in this proportion is sometimes added, not for adulteration but for preservation of the benzaldehyde, though the specific gravity of the oil is lowered thereby.

High specific gravity of the oil can usually be accounted for by the presence of a greater percentage of hydrocyanic acid than the 2 per cent. to 4 per cent. specification of the U. S. P. Schimmel & Company ("Schimmel & Company Report," April 1893) state that after the addition of 20 per cent. solution of HCN to a sample of oil of bitter almond of specific gravity 1.054, the gravity in two days had risen to 1.074. Oils containing up to 11 per cent. HCN have been known to reach a specific gravity of 1.096. The author has verified this fact in analyzing a commercial oil of which the specific gravity was 1.0688. The HCN content exceeded 6 per cent.

In studying oil of bitter almond, the author has been particularly interested in the benzaldehyde and hydrocyanic acid content. The methods given in the U. S. P. for the determination of both constituents of the oil are far from accurate as a consequence of indistinct end-points and the frequent formation of a precipitate before the end-point is reached. Gravimetric determinations, on account of the time required for complete precipitation and the subsequent drying of the precipitate, cannot be accomplished as quickly as the volumetric, but although the actual time spent by the analyst using the volumetric method is less, the results have to be checked as the worker feels uncertain of the end-point. Even then the results are not always satisfactory, as a rule, for the checks are not close enough to indicate the true value.

Where specifications for purity are given as in the U. S. P., it does not seem to be good judgment to put convenience ahead of accuracy. All volumetric methods available and modifications of them were tried out but in each case the checks obtained were not convincing as to the accuracy of a given method.

The following method is the one given in the ninth revision of the United States Pharmacopœia. The results of this method of analyzing four commercial oils are given in Table I.

TABLE I.

Sample.	Weight of oil.	Cc of $N/10$ $AgNO_3$.	Value of each cc $AgNO_3$ in grams HCN.	Grams of HCN.	HCN Per cent.
1	1.0769	7.40	0.0027	0.02001	1.85
	0.9271	6.64	0.0027	0.01836	1.93
2	1.0331	5.68	0.0027	0.01536	1.49
	0.4924	4.57	0.0027	0.01235	2.51
3	0.6073	6.88	0.0027	0.01859	3.06
	0.5309	7.05	0.0027	0.01909	3.60
4	0.6104	14.01	0.0027	0.03779	6.19
	0.6556	17.67	0.0027	0.04777	7.27

"Dissolve 15 Gm. of crystallized magnesium sulphate in enough distilled water to measure 100 mils, add 5 mils of this solution to 40 mils of distilled water, then add 5 mils of half-normal sodium hydroxide V. S. and two drops of potassium chromate T. S., and titrate the solution with tenth-normal silver nitrate V. S. to the production of a permanent reddish tint. Pour this mixture into a 100-mil flask containing about 1 gram of oil of bitter almond accurately weighed, mix well and titrate again with tenth-normal silver nitrate V. S. until a red tint, which does not disappear on shaking, is produced. Conduct this titration as rapidly as possible."

The first objection to the use of the foregoing method is the immediate formation of a precipitate. This, in itself, would not prevent the reading of an end-point if the precipitate coagulated nicely, but the solution remains cloudy and the precipitate becomes red before the surrounding solution does. Even with constant and vigorous shaking it is hard to be sure that the end-point taken is the true one. The color comes gradually and continues to disappear long after the point is reached which would be the end-point if a time limit of thirty seconds had been set. The results given in Table I are the nearest checks obtained from several consecutive determinations. In some cases the results had to be discarded entirely as the mixture darkened before any satisfactory reading could be made. The darkening was a result of the formation of silver hydroxide, possibly as a consequence of the concentrations of the mixture not having been worked out satisfactorily.

The following gravimetric method combines the best points of several suggested methods and works well. This method calls for little discussion since it presents no difficulty in manipulation. The results of the method tried on four commercial oils are given in Table II.

TABLE II.

Sample.	Weight of oil.	Weight of AgCN.	Equivalent weight of HCN.	Per cent. HCN.
1	1.7001	0.1398	0.02821	1.65
	0.5451	0.0404	0.008154	1.50
2	1.2519	0.0846	0.01707	1.36
	0.6401	0.0431	0.008699	1.36
3	0.3430	0.0561	0.011322	3.30
	0.6458	0.1028	0.020747	3.21
4	0.3085	0.1022	0.020626	6.68
	1.0510	0.3708	0.074825	7.12

One gram of the oil is weighed accurately in a tared, stoppered flask and dissolved in 15 cc of 95 per cent. alcohol. Ten cc of 10 per cent. ammonia water is added for the purpose of decomposing the phenyl-hydroxyacetonitrile which is formed in the oil by a direct reaction of benzaldehyde and hydrocyanic acid. 15 cc silver nitrate T. S. is added and subsequently the solution is acidified with nitric acid. The mixture is shaken until the precipitate has coagulated and it is then filtered on a tared Gooch crucible. The precipitate is washed with distilled water until free from silver nitrate and afterwards dried at 100° C. The crucible and contents are weighed, and the per cent. of hydrocyanic acid calculated from the following formula:

$$\text{Per cent. HCN} = \frac{\text{weight ppt.} \times 0.20182 \times 100}{\text{wt. oil taken}}$$

The gravimetric method is the most accurate and best for determining the hydrocyanic acid content.

The determination of the benzaldehyde content of oil of bitter almond is a more difficult problem. Much work has been done on the assay of the extract of the oil but little on the oil itself. Three methods were tried, the bisulphite, volumetric and gravimetric. The last-named method, which will be described further on, proved to be the only accurate one. The bisulphite method, checked against C. P. benzaldehyde, was discarded early in the experiment as the actual results were far from the theoretical values and there were no checks which could possibly be accepted as such.

In trying out the methods, C. P. benzaldehyde was used as the standard and the value of the method judged by the analysis of it. The volumetric method tried is the one given in U. S. P. IX, with the exception that 20 cc water was added before filtering the mixture. The method follows and the results are given in Table III.

TABLE III.

Sample.	Weight of oil.	Cc $N/2$ HCl for phenyl-hydrazine blank.	Cc of $N/2$ HCl added to oil plus phenyl-hydrazine.	Cc of $N/2$ KOH used in back titration.	Cc of $N/2$ HCl diff. between blank and sample.	Value of each cc. $N/2$ HCl in grams of benzaldehyde.	Per cent. benzaldehyde.
1	0.2990	21.22	36.39	20.48	5.31	0.05304	94.2
	0.4944	21.22	29.89	15.05	8.88	0.05304	95.26
	0.4782	22.10	24.91	11.73	8.92	0.05304	98.92
	0.5133	21.54	24.91	12.2	9.34	0.05304	96.51
	0.9213	21.54	24.91	18.4	16.44	0.05304	94.65
2	1.2370	23.09	31.70	28.68	20.07	0.05304	86.0
	0.6600	23.09	32.28	20.48	11.27	0.05304	90.57
	1.0879	22.79	28.97	25.60	19.42	0.05304	94.69
	0.3898	22.10	24.96	10.12	7.26	0.05304	98.65
3	0.7601	19.21	25.25	18.13	12.09	0.05304	84.36
	0.7546	22.6	20.2	8.42	10.82	0.05304	76.05
	0.7923	19.02	25.25	18.13	12.09	0.05304	80.93
	0.5583	19.21	25.25	15.06	9.02	0.05304	85.69
4	0.5555	22.10	24.91	11.84	9.03	0.05304	86.22
	0.4942	24.03	30.3	13.04	6.77	0.05304	72.66
5	0.7824	16.48	20.2	14.83	11.11	0.05304	75.31
	0.5859	20.2	18.31	5.05	6.94	0.05304	62.82
	0.7837	21.54	24.91	13.16	9.79	0.05304	66.19

"Dissolve about 3 mils of freshly redistilled phenylhydrazine in 60 mils of alcohol and titrate 25 mils of this solution, which must always be freshly prepared, with half-normal hydrochloric acid V. S., using methyl orange T. S. as indicator. To about 1 Gm. of the oil of bitter almond, accurately weighed, add 25 mils of the phenylhydrazine solution just prepared and allow it to stand for thirty minutes. Add a drop of methyl orange T. S., and acidify the mixture by adding a measured excess of half-normal hydrochloric acid V. S. Filter the mixture and wash the precipitate with small portions of distilled water until the washings cease to redden blue litmus paper. Then titrate the excess of hydrochloric acid in the filtrate with half-normal potassium hydroxide V. S. and subtract the number of mils of the half-normal hydrochloric acid V. S. consumed from the number of mils of the half-normal hydrochloric acid V. S. used in titrating the 25 mils of phenylhydrazine solution; the difference multiplied by 0.053 gives the weight of benzaldehyde."

In the method just described there is no end-point. The solution, before any indicator is added, is yellow and the change from yellow to red in the blank is very gradual. An arbitrary color change may be taken as an end-point on the blank but unless the titration is taken back and forth with half-normal hydrochloric acid and potassium hydroxide, there can be no certainty in the choosing of an end-point on the sample.

In using this method, it is always necessary to check the blank, either by adding a known excess of acid and titrating back or by titrating a fresh blank. The addition of water before filtering helps somewhat, but there is still a tendency toward cloudiness so that the final end-point is often obscured.

The values given in Table III are the results of consecutive determinations and are arranged in the order in which they were carried out in the laboratory. When the work was begun, it was thought that the end-point might be gradual because the wrong indicator had been used, so several others were tried. Thymol blue (p_H 1.2 to 2.8) was the only one which gave any satisfaction at all, but the results obtained with it were no more accurate than those obtained with methyl orange so that there was no apparent advantage in changing the indicator.

The results given in Table III are only those of determinations carried out uniformly in every respect. Variations were tried but as the results obtained showed no more accuracy than the others, no record of the results appeared necessary. Table III bears out the foregoing criticisms and indicates that the method is so inaccurate as to make it of little practical value.

The third and last method tried was the gravimetric method in which the benz-

TABLE IV.

Sample.	Weight of oil.	Weight of benzylidene-phenylhydrazone.	Weight of benzaldehyde.	Per cent. benzaldehyde.
1	0.1563	0.2791	0.15094	96.57
	0.2320	0.4179	0.2260	97.41
2	0.1152	0.1945	0.10519	91.31
	0.1448	0.2438	0.13185	91.06
3	0.2380	0.3823	0.20675	86.87
	0.1730	0.2812	0.15208	87.90
4	0.1817	0.2530	0.13683	75.31
	0.1072	0.1524	0.08242	76.88
5	0.1014	0.1349	0.07296	71.95
	0.1191	0.1575	0.08515	71.52

aldehyde is precipitated as benzylidenephenylhydrazone by phenylhydrazine. The method follows and the results of its use are given in Table IV.

The reagent for precipitation is made up as in the determinations of benzaldehyde in extract of bitter almond. Three cc of glacial acetic acid is added to 40 cc of water and mixed thoroughly. Two cc of freshly redistilled phenylhydrazine is added to this and the mixture again shaken.

Weigh accurately 0.1 to 0.15 Gm. of oil of bitter almond in a tared stoppered flask; dissolve in 10 cc of alcohol and add 15 cc of the phenylhydrazine mixture. Allow the mixture to stand in a cool, dark place for several hours. Add 200 cc of water and filter on a prepared Gooch crucible which has been previously weighed. Wash the precipitate freely with water and finally with 10 cc of 10 per cent. alcohol. Dry to constant weight in a vacuum desiccator over sulphuric acid or in a vacuum oven at 70° C. Weigh the Gooch and precipitate and calculate the amount of benzaldehyde in the sample according to the following formula:

$$\text{Per cent. benzaldehyde} = \frac{\text{weight of ppt.} \times 0.5408 \times 100}{\text{wt. of oil}}$$

It is most important in this method that the phenylhydrazine be freshly redistilled and be kept in a cool, dark place after distillation until ready for use. If the oil is dissolved in too much alcohol, the precipitate does not form well but this is easily remedied by the addition of a small amount of water. In case a larger amount of the oil is weighed, the amount of the phenylhydrazine mixture added should be increased 10 cc for each 0.1 Gm. of oil in excess of 0.15 Gm. This method is practically the one used by Denis and Dunbar (*Jour. Ind. and Eng. Chem.*, 1909) in analyzing almond flavoring extract. They found that it gave 97 to 99 per cent. of the theoretical yield and that benzoic acid or nitrobenzene did not affect the results. Results in Table IV show that 96 to 98 per cent. of the benzaldehyde may be determined by this method and checks may be made if desired.

SUMMARY.

1. The volumetric method of determining the hydrocyanic content of oil of bitter almond is unsatisfactory because of the impossibility of judging the end-point.

2. The gravimetric method for hydrocyanic acid works well, giving close checks.

3. The volumetric method for determining the benzaldehyde in oil of bitter almond is inaccurate, giving results from 94.2 to 98.9 per cent. on C. P. benzaldehyde.

4. The gravimetric method for benzaldehyde gives from 96 to 98 per cent. of theoretical value and is therefore more accurate.

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A METHOD FOR THE ESTIMATION OF ALOIN IN ALOES.

BY C. H. BRIGGS.

In the JOURNAL OF THE AMERICAN PHARMACEUTICAL ASSOCIATION, Volume 12, No. 8, page 695, Engelhardt and Crosbie call attention to the fact that there is no reliable method available for the estimation of aloin in aloes. Some twenty years ago the writer had occasion to assay aloes and devised a process which has been in use in this laboratory ever since. While this method is not ideal in that it is somewhat long and tedious, it serves as a very good indication of the amount of aloin which can be obtained from aloes in the commercial manufacture of aloin. It is with the hope that this method may be of service to others that it is offered for publication.

The method is as follows:

Dissolve 50 grams of powdered aloes in 300 cc of boiling water; to the solution add 4 cc of 25% acetic acid; mix well and allow to cool. Decant the clear solution into a 500-cc graduate and wash the resin with water by decantation or on a filter, according to its nature. To the filtrate add a solution of 10 grams of lead acetate (if the aloes is very black use 15 grams) in water and dilute to 500 cc. Shake well and filter with suction. Remove the lead from the filtrate by hydrogen sulphide and filter again with suction. Measure off exactly 400 cc of the clear filtrate representing 40 grams of aloes, concentrate *in vacuo* to about 30 cc; transfer to a 50-cc graduate washing out the flask with small portions of water until the solution equals 40 to 43 cc. Allow the aloin to crystallize for one day at ordinary temperature and then place in a refrigerator for another 24 hours. Filter with suction and wash crystals with a saturated aqueous solution of aloin until the mother liquor has been all washed out. Transfer crystals to a tared watch glass and dry. After weighing, the crystals should be exposed to the air for several hours in order that they may absorb hygroscopic moisture and then be re-weighed and thus furnish a representative assay of the aloin as ordinarily manufactured.

As this assay is dependent upon a process of crystallization, three duplicate assays should be made of each sample and the highest results reported.

ANALYTICAL DEPARTMENT,
PARKE, DAVIS & COMPANY,
DETROIT, MICHIGAN.
August 22, 1923.

THE TANNIN OF WILD CHERRY BARK.*

BY JOSIAH C. AND BERTHA L. DE G. PEACOCK.

In 1834, Stephen Proctor published in *The American Journal of Pharmacy* the results of an investigation which he had made of the constituents of wild cherry bark. In this report, besides the presence of certain other substances, he inferred that this drug contains tannin and gallic acid.

His analysis appears to have been made the basis of nearly every later reference by the textbooks to the constituents of this bark. But the presence of gallic acid has not been mentioned by all, nor would it likely be credited without question by any who consult the original article, for the inference was drawn contrary to the evidence afforded by an appropriate test—the iron salt he used gave a green color, not the blue one which gallic acid produces.

The astringency of wild cherry bark seems to have been attributed to "tannin," with little, if any, regard to possible presence of gallic acid.

* Read before Pennsylvania Pharmaceutical Association, 1923.

The list of constituents given for the bark almost invariably includes "a bitter principle."

While agreed on the source of the astringency, there has been a division of opinion regarding the substance which gives the bitterness. This property has been ascribed, in part at least, to amygdalin; or to a similar substance, but amorphous; or to an entirely different material. By some, the bitter principle has been considered to be the fluorescent principle.

Until the suggestion now made by the writers, no one has viewed the tannin as contributing bitterness as well as astringency; and only through isolation of the tannin could such conclusion well be reached.

Although Stephen Proctor pointed out that the tannin of wild cherry bark gave a green color and precipitate with an iron salt, the books have used the word "tannin" without reference to this fact, nor have they by other qualification distinguished this tannin from that so well known to pharmacists; while those references which have given gallic acid as a constituent have offered opportunity, if not indeed inclined, to the drawing of the incorrect inference that the tannin of wild cherry bark is tannin from which gallic acid is derivable.

It would be better if such uses of the word were more restricted or defined, especially since the United States Pharmacopœia gives the term "tannin" as synonym of Acidum Tannicum or Gallotannic Acid, and qualifies this use by stating that tannic acid is "a tannin usually obtained from nutgalls." Employment of the words "a tannin" is suggested, when mentioning the presence in drugs of substances of this class, particularly when the composition or characteristics are not sufficiently known to enable a statement which will differentiate from gallotannic acid.

The tannin of wild cherry bark has been blamed for most, if not all, of the troublesomeness of the preparations of this drug. It has been customary to say that certain menstrua extract more or less of the tannin; the opinion in general being that the less tannin removed the better the taste and keeping qualities of the preparation. The color of the cold-water infusion has been thought to be darker or lighter as the amount of the tannin was more or less. The addition of glycerin to the water used for percolating the drug in the preparation of the syrup has been opposed by some on the ground that this addition extracts more of the tannin, while others have insisted that only by this use of glycerin can a satisfactory product be had.

The tannin has been estimated by several investigators, who have employed different methods. Its amount is given as varying from 2.5 to 4.5 per cent. By some it is stated to be most abundant in autumn, while others find that "in the spring when the bark is least valuable it is richest in the tannin." The U. S. P. IX defines wild cherry bark as "the stem-bark of *Prunus serotina* Ehrhart (*Prunus virginiana* Miller) (Fam. Rosaceae), collected in autumn and carefully dried."

An estimation of the tannin in the ground bark used in this work was made by the hide-powder method. This determination, which is regarded as only approximate, showed 3.33 per cent. for the air-dry drug. Loss upon drying to constant weight amounted to 2.14 per cent.; which, taken for the purpose as moisture, would indicate 3.4 per cent. of tannin in an absolutely dry sample.

A striking feature which was recognized in the application of this method of estimation was the fact that one-third of the total hot-water soluble matter taken from the bark was absorbed by hide. It was found impracticable to make a complete extraction of the cold-water-soluble solids before evidence of change became noticeable in the liquid. Such relatively large representation of the soluble solids and the readily alterable nature of the tannin make very evident the potentialities of this constituent for trouble in attempts to make and preserve uniform preparations of this long-used drug.

Our intention in undertaking this work was to extract and purify the tannin in order to learn something of it as an isolated substance. To obtain the tannin, a quantity of ground wild cherry bark was moistened with cold (but not distilled) water, macerated for twenty-four hours, and percolated with same solvent until the liquid coming through was pale yellow. The percolate was concentrated by evaporation until a dark wine-red liquid resulted. This was allowed to cool, and was then freed by filtration from the insoluble matter which separated during concentration; this was composed very largely of phlobaphene, but there was present also a decided showing of microscopic octahedra of calcium oxalate (a substance long known as present in the bark). Aside from determining the phlobaphene nature of the bulk of the insoluble matter, no further attention was paid here to these substances.

The clear filtrate was shaken with acetic ether to remove the tannin; the solvent layer was collected and distilled under reduced pressure in order to get the tannin as a solid.

THE PRESENCE OF BENZOIC ACID.

In the last-named effort, it was found that the presence of some accompanying substance was preventing the tannin from "puffing" into the porous or spongy condition usually assumed at the stage of the distillation when all but a little of the acetic ether has been driven off. Upon continued application of the water-bath heat to thoroughly dry the residue which had been obtained, white flakes of feathery crystals were observed to be accumulating on the cork and in the delivery tube. Their behavior and form was so immediately suggestive of benzoic acid that for the moment our attention was diverted to a review of the circumstances which would permit benzoic acid to be present. Until this interference, we were unacquainted with the occurrence of benzoic acid in wild cherry bark. But, in 1909, Power and Moore reported finding benzoic acid and a number of other substances not previously known to exist in this drug. (See *Jour. Chem. Society* (English) (95), 1909, page 243; or abstract in PROC. AMER. PHARM. ASSOC., 1910, page 208.)

Our reflection ran as follows: why might not benzoic acid be present here, since it results from oxidation of benzaldehyde, and this tendency of benzaldehyde is a constant proclivity? Benzaldehyde was present in the original percolate, but not, if judged by odor, in the concentrated liquid. Perhaps it has been oxidized to benzoic acid, but here is evidence of a much larger amount of the acid than that source and change could supply even if all of it were oxidized, which is unlikely, because a portion would have been volatilized unchanged from the liquid as this became warm. From where, then, does this amount of it come? The simultaneous production of benzaldehyde and hydrocyanic acid when the bark is moistened with water is well proved. There has been widely quoted the statement that the dry

bark of commerce does not contain either hydrocyanic acid or benzaldehyde, and an examination of the dry bark, without moistening, strengthens this impression. However, Stevens while collecting the bark found it to have an odor of bitter almond. In this instance, the odor would scarcely be attributed entirely to hydrocyanic acid, but rather to both it and benzaldehyde as the products of the well-known reaction which takes place when the dry bark is moistened; for is not the bark on the tree functioning under the influence of its life moisture, its sap? The removal of the bark interrupts the plant process by discontinuing the moist condition essential to it. The loss of the odor of bitter almond when the fresh bark is dried must be due to volatilization of the hydrocyanic acid and benzaldehyde, or to alteration into something which differs in odor. The extremely volatile hydrocyanic acid may well be regarded as dissipated with little or no change, but the less volatile benzaldehyde would be inclined to undergo more or less oxidation to benzoic acid, besides in part passing off unchanged. And, is it not likely that this change is in constant operation in the living bark, with production and accumulation of benzoic acid therein? As regards the detached bark, the contained benzaldehyde perhaps dries off in part, but because its comparatively minute quantity is through relatively wide distribution so effectively given surface exposure, it is quite as likely oxidized *in situ* to benzoic acid. This conception appears as highly probable, indeed. Again, when the dried bark is chewed, or otherwise moistened, with cold water, does not the bark merely resume (to the extent possible with the now limited supply of the essential materials) the production of the substances which gave the living bark its odor of bitter almond? Therefore, would not the bark when collected probably contain benzoic acid, and would not the amount of this be increased by permitting the interrupted process of its production to resume by restoring the moisture necessary to this function? These crystals might well indeed be benzoic acid.

And subsequent examination showed them to be benzoic acid.

The foregoing thought led also to recognition of the probability that benzoic acid may well be expected to be found in every plant substance, wherein benzaldehyde has existed—the scope of which suggestion points to many possibilities of its occurrence.

In further examination of the thought that the greater part of the benzoic acid must exist prior to concentration of the percolate, it was recalled that considerable needles of benzoic acid had been observed to separate when some of the final portions of the water percolate, which had come through with but little color, had been boiled down. Their appearance was made long after the odor of the percolating liquid had ceased to suggest the presence of benzaldehyde. But, to learn of the possible influence of the heat used for evaporation of the percolate as a factor in the production of benzoic acid, another lot of the ground bark was macerated and percolated with cold water. The percolate was not concentrated, but at once shaken with acetic ether. The amount of benzoic acid which was encountered in this process was apparently as great as that in the case of the concentrated percolate. It thus became more evident that the bulk of the benzoic acid exists in the bark before the moistening process.

Finally, the existence of free benzoic acid in the bark was proved by direct extraction with ether and with chloroform; removal of solvent; treatment of ex-

tracted matter with water; shaking of aqueous solutions with ether and with chloroform, and separation and evaporation of these solvents.

Returning to the process of extraction of the tannin from the concentrated percolate, the residue left upon evaporation of the acetic ether was, at first, red, resin-like in appearance, nearly transparent, but, when it had become cold, was found to be largely composed of needle-shaped crystals. Each successive shaking of the concentrated percolate with acetic ether gave a similar mass; and these residues gradually showed an increasing proportion of the crystals. These residues were stirred with cold ether for the purpose of removing from the tannin such substances as would be dissolved. The greater part of the benzoic acid entered solution. Along with it, the ether dissolved an appreciable amount of a plastic, red material. When warm, this substance seemed to mix with the benzoic acid in such way as to obscure its crystals; but when cold, the needles became plainly visible throughout the plastic, resin-like material. Boiled with water, this mass gave up benzoic acid, which readily crystallized from solution upon cooling; but not without the red portion entering solution to a considerable extent, for concentration of the reddish liquid so obtained resulted in the settling out of a dark red substance, which, when cold, varied in consistency from fluid to semi-solid.

Both the hot- and cold-water solutions of the ether-dissolved substances displayed decided fluorescence. No further work was done on the last-named materials.

Under treatment with cold ether, the residue containing the tannin took at first the form of a granular, red, porous powder; but with accumulation of moisture, through constant condensation brought about by the cold resulting from evaporation of the ether, the undissolved matter became plastic. To relieve this situation, the residue was redissolved in acetic ether, and reobtained by distilling off the solvent *in vacuo*. This material was then stirred with cold chloroform; to appearance, it removed a trifle of yellow color. Upon recovery, the chloroform left an oily looking liquid. When this liquid was boiled with water, it separated into much benzoic acid and a small amount of oily drops. The solutions so obtained showed much fluorescence. Beyond identifying the benzoic acid, nothing was undertaken with these materials.

When the now partly purified tannin had dried free from chloroform, it was found to be a finely divided, reddish yellow powder. This powder was treated with water which left a considerable undissolved portion. The aqueous solution was clarified by means of paper pulp and filtered. The clear reddish amber solution was shaken with acetic ether, its layer separated and the solvent removed by distillation *in vacuo*. The residues thus had were subjected to separate successive treatments with ether and chloroform as outlined; after which, the tannin was again dissolved in water, and the whole process of purification repeated over and over, until the ether and chloroform failed to remove appreciable matter.

Judging by the bulk of benzoic acid which separated as this work was carried on, it is felt that there may be quite as much of free benzoic acid in wild cherry bark as there is of the tannin. Though now but speculation, the possible presence of benzoates also is a matter for investigation.

The many repetitions of the foregoing process of purification finally gave the tannin in straw-yellow or faintly pinkish porous masses, with satiny luster or

highly iridescent effect; these spongy masses were readily reducible to powder. The variations in color depended upon the extent of alteration which had occurred when the acetic ether solution was evaporated *in vacuo* to obtain the tannin in solid form. Snow-white porous masses which at first formed in the distilling flask, when the solution in acetic ether had reached a degree of concentration where solid showed above and about the boiling liquid, are believed to indicate the true color of this tannin; but, while the vaporization of the last portion of the solvent was being effected, the color of these masses changed to straw-yellow or faintly pinkish, it is thought, because of slight decomposition of the solvent with production of acetic acid, which is now known to exert an altering effect on the tannin. And it does not seem improbable that traces of benzoic acid, still adhering, caused or increased this behavior of the acetic ether, or this effect upon the tannin. It was not found to be practicable to disconnect the flask and remove the white masses, for immediate condensation of the acetic ether vapor caused their instant disappearance through solution. Nor did there seem to be any other way of overcoming this objectionable action which invariably rendered part of the tannin insoluble in cold water.

The tannin of wild cherry bark extracted and purified by the given method is a bitter as well as astringent substance. It was readily and completely soluble in hot water; when treated with cold water, a quantity entered solution, at once, imparting an amber color, while a greater amount remained undissolved as a peculiar, plastic phlobaphene. The one per cent. solution made with hot water had an amber color. Solutions of the tannin in hot water, when allowed to cool, acquired yellowish turbidities. Both hot- and cold-water solutions gave white precipitates with gelatin. When cold, the solutions of the tannin gave dark green colors and precipitates with ferric chloride and ferric acetate, the green shades becoming blackish on standing, or upon use of excess of reagents. Lead acetate caused a canary-yellow precipitate in the solutions. The solution of the tannin, like the substance itself, had both bitter and astringent tastes, which were appreciable in this order of effect, the bitterness was experienced first; it persisted, almost to the exclusion of the astringency, which was felt only after the bitterness had passed; recurrences of the taste seemed to be entirely those of bitterness. Blue litmus paper was intensely reddened by the solutions. The amber colors of the solutions were destroyed by addition of either diluted sulphuric, oxalic or benzoic acid; no fluorescence was manifested thereupon. When portions of solution, acidified with these acids, were heated in a boiling water-bath, reddish colors developed, and later red substances were deposited. As control, an unacidified portion of the tannin solution showed only the slightest reddening. This or a similar change was found to take place with benzoic acid even in cold dilute solutions, after a few days' standing. This effect of benzoic acid on the tannin is noteworthy by those concerned with the preparations of wild cherry bark.

Six per cent. acetic acid, at first, behaved toward the tannin like cold water, but soon dissolved the substance entirely. Furthermore, the insoluble substance produced by contact with water was found to be at once dissolved by six per cent. acetic acid. When solutions made with acetic acid were heated on a water-bath, no precipitation took place, but their amber colors were reddened. Both weak and strong acetic acids dissolved the red substances referred to above as produced by the action

of diluted sulphuric, oxalic or benzoic acid. The tannin was at once freely soluble in 36% acetic acid with formation of amber-colored solution; dilution of this fluid, or of any other containing acetic acid, with water did not cause precipitation. The tannin was readily soluble in alcohol, weak or strong; insoluble in ether free from alcohol, otherwise soluble; insoluble in chloroform or benzol. The tannin was freely soluble in glycerin, as were also both water-produced and acid-produced insoluble red phlobaphenes; these glycerin solutions remained brilliant upon dilution with water.

When the tannin had been found to be bitter as well as astringent, attention turned to the question whether this constituent contributes all or but part of the bitterness of the drug. In an effort to get information on this matter, infusions of the bark (some representing as much as 30 per cent. of the drug) were treated with well-washed hide-powder. The following facts were noted. Before maceration with hide, the freshly prepared infusions (light wine-red or reddish amber in color, when viewed in half-liter flasks) were immediately and decidedly acid to litmus paper; pronouncedly bitter and astringent as already described. After maceration with two successive treatments of hide-powder, these liquids, except for the distinct blue fluorescence, were almost entirely free from color; the odor was changed, but not removed; acidity to litmus paper was shown only upon standing; neither bitterness nor astringency could be detected; ferric chloride gave but the slightest greenish tinge that could have been discerned; there was no precipitate with either gelatin or lead acetate solution.

These treatments with hide-powder were made on infusions prepared with both hot and cold water, but the hot liquids were allowed to cool before being brought into contact with the hide. The results were uniform when the infusions were used without delay; but not so when old infusions were treated. A single treatment with hide-powder did not appear to effect complete removal of the tannin within a period not likely to admit of the variance just referred to as attendant upon delay. The several steps in the treatments with hide-powder were controlled by using an equal amount of this material with water alone. All detannated liquids were filtered before results were noted.

Some of the filtered, clear, fluorescent liquid from the hide treatment was shaken with chloroform; the layer of the latter separated, and the solvent evaporated. A small amount of white crystalline residue was obtained. This was but sparingly soluble in water; the solution displayed blue fluorescence. Upon the addition of ammonium hydrate, to alkalinity, a very high degree of fluorescence resulted. Appearances, however, pointed to the probability that the greater part of the crystalline residue was benzoic acid. The natural fluorescence in the infusions of the bark, or other solutions which exhibit it, should not be confused with like phenomena artificially brought about with outside agents, such as alkalies.

Because of the presence of so much calcium oxalate in the concentrated percolate, an effort was made to learn if free oxalic acid was present in the bark. To avoid any opportunity for it to combine with calcium or other bases, distilled water was used to percolate the bark. After concentration, the liquid was detannated by maceration with well-washed hide-powder, filtered, then made alkaline with ammonium hydrate, again filtered, then acidified with hydrochloric acid, again

made alkaline with ammonium hydrate, acidified now with acetic acid, and tested with calcium acetate solution. There was no precipitation by the calcium compound at this point to indicate the presence of oxalates; but that the conditions were favorable to their detection was proved by a control test, which, besides other matters, took into consideration the presence of free benzoic acid in the solution. The result of the experiment would seem to indicate that uncombined oxalic acid is not present in the bark.

GALLIC ACID NOT PRESENT.

As ferric chloride caused no blue color in the infusion after the latter had been detannated, the absence of gallic acid is regarded as now proved, especially since the addition of a minute amount of this substance, by giving the characteristic blue color, showed that conditions were favorable to its detection. Gallic acid should, therefore, be omitted from the list of constituents of wild cherry bark.

That the fluorescence of the infusion was not removed by hide-powder while the astringency and bitterness were completely absorbed are facts clearly established by that treatment; and, since fluorescence remained in the fluid from which all bitterness and astringency had been removed, it seems proper to regard the sources of these properties as different. Again, since the purified tannin was bitter as well as astringent, and no bitterness or astringency remained in the fluid from which all tannin had been absorbed (as proved by means of ferric chloride, gelatin and lead acetate), the conclusion that the tannin furnishes all of the bitterness and astringency seems justified. And, if, in the light of the determined characters of the tannin of wild cherry bark, we review the descriptions of efforts which have been made to isolate "a bitter principle," and compare the comments on the observed nature of the substance sought, there seems to be every reason to believe that, because of the inherence of bitterness in the tannin, it has all of the qualifications needed to elude isolation by the methods which have been employed to find another substance representative of this property of the drug.

The tannin of wild cherry bark having been found to be bitter, there arose the question: Is it the bitter tannin found in red and pale rose petals—the drugs coming from the same natural order of plants? The answer is in the negative, for the tannin of wild cherry bark does not yield the peculiar burr-like aggregates characteristic of the rose tannin when its solution is boiled with acids.

SUMMARY.

The results of this work may be summarized as follows:

Gallic acid is not present in wild cherry bark.

Cold water extracts only part of the tannin, for there is also a considerable proportion of cold-water-insoluble phlobaphene.

The tannin of this bark, as pointed out by Stephen Proctor, is an "iron-greening" tannin.

This tannin yields a red phlobaphene by action of acids, including that of benzoic acid.

There is a considerable proportion of free benzoic acid in this bark, the occurrence of which was first reported by Power and Moore.

The occurrence of benzaldehyde in living plant material may well be taken as indication of possible presence of benzoic acid in any subsequently dried form of the part.

The tannin is the bitter principle as well as the astringent constituent.

The bitter principle, which is the tannin, is not the fluorescent principle.

It permits of better understanding of the troublesomeness of the preparations of wild cherry bark to know that the free benzoic acid contained in the drug decomposes the cold-water-soluble tannin with production of cloudiness or sediment; and, because of this action, the blame, which in the past has been placed entirely upon the tannin, may now be equally accorded to the benzoic acid.

The addition of glycerin to the water used for extraction of the bark in the preparation of the syrup will now be fully appreciated as warranted by the association in the bark of the tannin and benzoic acid, as well as by the teaching of experience with its use.

Also, due allowance must be made for variation in the products of those vegetable drugs which bring into the course of preparation the resumption of an interrupted plant process. For this reason, variation in the preparations of wild cherry bark must be expected, even though glycerin or acetic acid (both solvents for the decomposition products of the tannin by the benzoic acid) or both, be employed in the menstruum.

A STUDY OF PACIFIC COAST PEPPERMINT.

BY C. W. JOHNSON AND ROBIN WILKES.

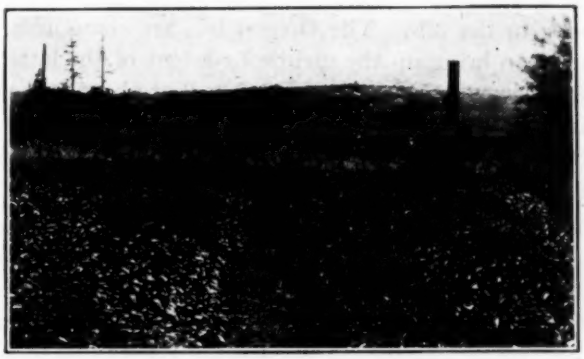
During the last two years a study of Pacific Coast peppermint has been made at the University of Washington. This study was made to show the advantages that Washington and Oregon have over eastern states in the production of peppermint oil. The age of the industry in the northwest is very young, but old enough, especially in Oregon, to show us that it is a very profitable and promising industry in these parts of the United States.

The peppermint industry appears to have been introduced into the United States by the early settlers of New England. The plants were first grown in Wayne County, New York. Then gradually the industry extended west to northern Ohio and from there into Indiana and Michigan. At the present day there are about 25,000 acres under mint cultivation in the United States, nearly all of which are in the states of Michigan, Indiana, New York and Oregon. This country furnishes about 250,000 pounds of peppermint oil yearly and, at the present time, we also import 88 per cent. of Japan's crop.

Peppermint was first introduced into Oregon about 1908 by Mr. O. H. Todd of Eugene and it has been produced in the state for the last fifteen years. Mr. Todd imported the roots for the first planting from England. Oregon is especially adapted to peppermint cultivation because it possesses the valuable and rich beaver-dam land of the Willamette Valley. This swamp-like land is rich in humus and retentive of moisture but fairly open in texture and when well drained, either naturally or artifically, is most suitable for peppermint cultivation. The district of Lake Labish contains several hundred acres of this type of land. The average

yield of mint oil per acre in this district is 70 lbs. In 1922 a little more than 300 acres in the Willamette Valley were under peppermint cultivation. During the last season, of 1922, two acres of the mint produced 186 lbs. of oil or 93 lbs. per acre. This is an extremely large yield. In a statement from G. J. Moisan, secretary of the Oregon Mint Growers Coöperative Association, he reports that the season of 1922 was very dry in the Willamette Valley and the yield on some of the land was very small, yet the returns were far better than they would have been for grain or hay. About 12,000 lbs. of single distilled oil were produced on the 300 acres in 1922. Tests have demonstrated that good bottom land almost anywhere in the Northwest will yield 50 to 60 lbs. per acre in a normal year.

These broad level stretches of land are easily tilled because large horse tools can be used. In the spring when the soil is usually very soft it is necessary to use mud shoes 9 or 10 inches wide on the horses. These shoes are generally made of wood and leather and fastened by straps and metal bolts to the hoofs or ordinary shoes of the horse. Planting begins as early in the spring as possible and the harvesting of the mint starts in August when the plants are in full bloom. It has been said that due to the early spring in Oregon the growers there should be able to get their product on the market before the Michigan growers and so profit by the higher price offered for the first oil. Only three crops can be raised on the sandy river-loam type of plantation while on the rich muck-land, peppermint can be grown year after year for five or six successive years before it becomes necessary to plant the field with something else.



This picture shows two beds of peppermint in the Garden of Medicinal Plants, University of Washington. The plants on the right came from New York and those on the left from a producer in Oregon.

A number of varieties of mint have for the last six or seven years flourished in the Garden of Medicinal Plants of the University of Washington. The plantings came from different parts of the country, some from New York, some from various producers in Oregon and one bed from a producer in the southern part of the state of Washington. There are thirteen plats in all covering an area of about 3600 square feet.

Most of these beds have been harvested for the last two years and the oil analyzed. The herb was cut and allowed to partially dry and then stems were

again cut into small pieces and steam-distilled. The still used at the University of Washington was very inadequate, for its capacity was far too small to care for the herb as it dried. After numerous distillations small amounts of oil were obtained from three varieties. The yields were not very large due probably to the poor facilities for handling and the fact that the mint has grown on the same plot of ground for about seven continuous years. The aqueous distillates were cohobated and this increased the volume of the oil about 6.5 per cent.

Samples of the 1921 crop of oil were secured from seven different producers in Oregon. These oils and also the oils from the Garden of Medicinal Plants at the University of Washington were analyzed for their menthyl acetate and total menthol content and in each case it was found that they assay considerably higher than eastern oils in both menthyl acetate and total menthol. One Oregon oil ran as high as 78 per cent. total menthol which is more than twice as high as the average Michigan oil. The average total menthol content of Oregon oils was found to be 62 per cent. The Oregon products are also very high in ester content, menthyl acetate averaging about 10 per cent. It is this compound that gives most of the fragrance and odor to the oils. The Oregon oils are sometimes mixed with the eastern oils in order to bring up the menthol content of the latter to standard of the United States Pharmacopœia. Oregon oils sell at about 50c. more per lb. than Michigan, Indiana or Illinois products, because they run much higher in menthol and menthyl acetate. The specific gravity of the western oils ranges from 0.8995 to 0.9436, averaging 0.9147, and the refractive index varies from 1.4600 to 1.4665. The optical rotation also is quite variable, ranging from —23.5824 degrees to —36.414 degrees.

The comparative analyses are shown on the chart below.

CONSTANTS OF OREGON AND WASHINGTON PEPPERMINT OILS.

Producer and location.	Menthyl acetate, per cent.	Total menthol, per cent.	Refractive index, 20° C.	Optical rotation.	Specific gravity, 15.6° C.
Claud Bevens, Lake Labish, Oregon No. 1	15.5	78.45	1.4600	—32.5994°	0.9070
Wilson and Davies, Independence, Oregon No. 2	15.08	77.24	1.4617	—29.1312°	0.9130
O. B. Marshall, Albany, Oregon (White mint) No. 3	10.28	73.04	1.4630	—27.7440°	0.9065
O. B. Marshall, Albany, Oregon (Black mint) No. 4	9.85	70.19	1.4620	—29.4780°	0.9030
Mrs. L. Hayes, Eugene, Oregon No. 5	7.90	59.99	1.4615	—23.5824°	0.8995
G. J. Moisan, Gervais, Oregon No. 6	13.60	63.82	1.4633	—36.414°	0.9218
E. B. Wallace, Albany, Oregon No. 7	9.37	61.20	1.4665	—26.875°	0.9436
Drug Garden, Univ. of Washington No. 8	12.12	68.73	1.4647	—31.216°	0.9113
Drug Garden, Univ. of Washington No. 9	20.46	63.84	1.4660	—28.3720°	0.9292
Drug Garden, Univ. of Washington No. 10	11.31	64.43	1.4653	—29.3210°	0.9156

A different indicator than that used in the United States Pharmacopœial assay of total menthol and menthyl acetate was used in the analysis of these western oils. The regular U. S. P. assay was followed in every other respect excepting this one; the indicator, phenolphthalein, was changed for phenol red. It was found in the determination of menthyl acetate and total menthol that phenolphthalein was not very satisfactory due to the fact that its colorless acid reaction was masked by the yellow color of the saponified oil. The characteristic color of an acid reaction to phenolphthalein should of course be colorless; because of the covering up of the acid reaction to phenolphthalein the end point is difficult to determine. Of the various other indicators used phenol red was found to be the most satisfactory. It gives a pink or red color, according to the concentration of the indicator, when alkaline, and a canary-yellow when acid. This yellow color shows up very distinctly and is not in any way interfered with by the color of the saponified oil. It is also a very sensitive indicator, one drop of either acid or alkali changing the color completely from pink to yellow, or vice versa.

In all ten samples analyzed the percentage of menthyl acetate and of total menthol ran very high as compared with the eastern oils of this country. The western oils assay more nearly like the Japanese and European oils. Perhaps western climatic conditions are responsible for the high menthol and menthyl acetate content. It has been shown by Umney and others that the climate and soil both have a considerable influence on these two constituents and it is thought that such is the case in Oregon and Washington. The air is very humid in both of these states throughout the summer and there is not the hot drying effect which is found in some of the eastern localities where peppermint is grown. This humid climate is probably one of the factors that cause the large yield of oil and the high percentage of menthol and menthyl acetate in the peppermint oil of the Northwest.

LABORATORY OF PHARMACEUTICAL CHEMISTRY,
UNIVERSITY OF WASHINGTON, SEATTLE,
June 27, 1923.

CHEMICAL EDUCATION IN PHARMACY SCHOOLS.*

BY JOHN C. KRANTZ, JR.[1]

The schools of pharmacy holding membership in the American Conference of Pharmaceutical Faculties offer two well-defined courses. The first course covers a period of two years and is especially intended to train students for the intelligent practice of retail pharmacy, *i. e.*, the filling of physicians' prescriptions and the manifold other duties demanded of the pharmacist of to-day. The second course, which covers a period of three years, is intended to prepare students for the fields of analytical and manufacturing pharmacy, food and drug analysis work, etc. Many schools of the larger universities, however, offer advanced courses leading to the bachelor's, master's and doctor's degrees in pharmacy. The chemistry to be taught in the two-year course will be the chief consideration of this paper.

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The field included by pharmaceutical chemistry is very extensive, and, in a broad sense, may be defined as the chemistry of all products used as medicines. One immediately realizes that such a field requires a thorough grounding in fundamentals of inorganic and organic chemistry, in addition to the application of the science to pharmacy.

There are essentially two great dangers in the teaching of chemistry in pharmacy schools; first, the danger of making the course so general that it loses all of its pharmaceutical application and consequently the attention of the student; the second danger is the strictly applied course, in which the student fails to catch the vision of general chemistry and ultimately his chemical education becomes stinted by the boundaries of pharmacy.

There are many advantages and disadvantages that may be cited by making a careful analysis of both the general and applied methods of presenting chemistry to pharmacy students. The general method, which is of course the teaching of arts and science freshman and sophomore chemistry, gives the student a broader vision of the science and in many ways establishes a definite relationship between chemistry and the every-day life of the student, which is quite impossible to do when teaching applied chemistry. General chemistry has a cultural value that is lacking in the applied science and has an intrinsic value when wanted for use as college credits in academic schools and for premedical work. The outstanding disadvantage, which partially overshadows the advantages mentioned, is that the average pharmacy student fails to make the connection between the general science and those parts which are important pharmaceutically and very often puts the emphasis in the wrong place. Then again, general college chemistry in many instances is incomplete for pharmaceutical purposes. Thus the production of disodium hydrogen arsenate is of utmost importance to the pharmacy student and yet only mentioned in passing in general chemistry courses. Other cases could be cited which would show how this type of incompleteness of general chemistry would severely jeopardize the education of the pharmacist.

The teaching of strictly applied pharmaceutical chemistry is, in a broad sense of the word, an injustice to the student unless the course be called pharmaceutical chemistry and not just chemistry. Without the general view of chemistry the student not only misses the viewpoint of the chemist but is likely to think that the sole purpose of chemistry is to serve the pharmacist. This applied chemistry has little cultural value and is not usually accepted for credit in academic or premedical schools. Thus, if a student having completed a two-year pharmacy course, in which strictly applied chemistry is taught, wished to get the degree of bachelor of arts, he would find it necessary to repeat a large amount of the work done in chemistry in order to secure proper credit for it.

Enterprising pharmacists, however, have suggested a loophole to this serious chemical dilemma, which in the author's experience in the School of Pharmacy of the University of Maryland has proved most successful in obviating the above-mentioned difficulties. It was pointed out that the objections to the general and applied methods of teaching chemistry are caused by extremes in both directions. This being true, if the lecturer teaches general chemistry and presents the point of view of the chemist and the director of the laboratory director be a pharmacist, both may go as far as they like in their particular fields and the ultimate outcome

would be a student, both generally and pharmaceutically developed in chemistry. The lecturer should be a man who did not receive any portion of his training in a pharmacy or medical school, as this kind of training tends to cause the lecturer to make pharmaceutical applications in order to arouse interest in the student and neglects his principal mission of creating a vision of chemistry and giving the student a thorough drilling in the general principles underlying the science. On the other hand, experience has shown that it is not objectionable for the laboratory director to have chemical training above that which is necessary to become a pharmacist and, as a matter of fact, this is very often desirable. The additional training aids the instructor to connect the general principle with the specific case and will, if properly correlated, impress indelibly in the mind of the student that the lecture and laboratory courses are inseparable and both have the same aim, *i. e.*, the chemical education of the student.

The content and purpose of the laboratory and lecture courses make it necessary for both men to coöperate to the last detail in order to properly cover the required curriculum. To illustrate, after the lecturer has expounded and elaborated the valence and oxides of phosphorus and shown its numerous commercial applications, the laboratory man preceding the laboratory experiments will discuss very fully the pharmaceutical applications of the acids of phosphorus, the importance and reactions of the alkali phosphates and just why the student of pharmacy should center his time and attention at this point. After the discussion of the position of arsenic in the periodic table and the general chemistry surrounding this important element by the lecturer, the laboratory director will point out just why certain pharmaceutical preparations require alkali bicarbonate to dissolve arsenous oxide and why in other cases hydrochloric acid is used to effect the same. The director of the laboratory will have the student carry out the arsenic test as recognized by the United States Pharmacopœia instead of following some general text. After the mastering of systematic qualitative analysis scheme the student is given unknown specimens which are of a pharmaceutical nature yet illustrate and point out the use of the qualitative scheme. In many cases the Pharmacopœia demands the absence of or limits the amount to be present of certain impurities in drugs; here again the laboratory director uses this opportunity to connect qualitative analysis with the every-day operation of the pharmacist. Thus the detection of the presence of lead and sulphuric acid in citric acid is very interesting and instructive to the student, as the purity of the product he sells means the reputation he will establish in his community.

In the second year's instruction after the lecturer has given the student an intelligent conception of the alcohols, the director of the laboratory then carries out his part of the program by pointing out the importance of alcohols to pharmacy, the impurities likely to be found present and the Pharmacopœial tests for purity. In organic chemistry the laboratory man must devote more time to lecturing than in inorganic chemistry and should follow up each class of organic compound with lectures on pharmaceutical products that occur in that particular class. Thus under the sulphur derivatives of the ketones the pharmacist has a list of hypnotics—trional, sulphonal, etc.—the structure of which and method of preparation are extremely important to pharmacy students. Instead of having the student extract caffeine from tea or coffee as is usually done in general chemistry

courses, the pharmacist substitutes Guarana, the crushed seeds of a Brazilian plant, which is used as a stimulant and nervine in medicine and contains 4% of caffeine.

Quantitative chemistry presents a very striking example of this method of teaching the science. The lecturer may or may not deal with the theory of quantitative chemistry; in the author's experience it has been found advantageous to allow the laboratory director to handle the subject of quantitative chemistry after the lecturer has given the student the general chemist's point of view on the subject. In this course, the Pharmacopœia in its many assay processes offers an example for practically each type of analysis made in an elementary course. The halogens are estimated by the Pharmacopœial method, aluminum as oxide from the official alum iron by the dichromate and permanganate processes in pharmaceuticals, morphine from opium and many other applied, yet comprehensive experiments.

The chemistry of the advanced courses are of course taught with the aim of making the student proficient in the particular branch he has chosen. In the third and fourth years physical and physiological chemistry are taught in addition to advanced qualitative and quantitative work with food and drugs.

This plan of presenting chemistry to pharmacy students has in its entirety proved practicable and successful in the Pharmacy School of the University of Maryland and will, if conducted properly, accomplish a two-fold purpose: First, to give the student as broad an aspect as possible of the science of chemistry and, second, to give a course in chemistry that is useful and applicable to pharmacy.

Delegates to the International Pharmaceutical Federation—London, England.

Sitting—front (from left to right)—Dr. J. J. Hofman (Secretary), C. L. Butchers (Australia), Prof. Van Itallie. (President), J. Loisel (France), A. Van Den Dries (Holland).

Second Row—A. Langrand (France), D. H. Lacroix (France), Cav. F. Pratta (Italy), M. Pattou (Belgium), Dr. A. Schamelhout (Belgium), W. A. Carter-Ross, W. A. Carter (Shanghai), E. Collard (France).

Third Row—V. Van Itallie (Holland), Mr. W. B. Falding (London), Dr. Angel Morales (Spain), Dr. A. Bouville (France).

Back Row—Sir Wm. Glyn-Jones, Mr. V. Cofman, Cav. Dr. A. Robaldo (Italy), Mr. Ed. White, M. Rousseau (France).

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A GARDEN OF HERBS.*

BY CASWELL A. MAYO.

On becoming a flat dweller in Cincinnati I was forced to fall back on the front yard of the laboratory of the Wm. S. Merrell Company as the only available piece of ground which I could convert into a garden. This the firm kindly placed at my disposal together with a liberal appropriation for expenses and here we have the beginning of a "Garden of Herbs" which promises to be of considerable interest.

Prior to the Civil War Cincinnati was the center for the collection of indigenous drugs. But now this center is in the mountains of North Carolina. Within twenty-five miles of Cincinnati I have found forty or fifty medicinal plants some of which, such as Hydrastis, have been almost entirely wiped out by the drug collector.

The intensive cultivation of the land constantly reduces the areas where indigenous drug plants can be found while commercial diggers soon clear out of such woods as are left near the cities the more valuable drugs for which there is a ready market.

In Hamilton County, Cincinnati, Ohio, and Kenton and Campbell Counties, Kentucky, just across the river the following drug plants were indigenous but have been exterminated:

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* Scientific Section, A. Ph. A., Cleveland meeting, 1922.

Eupatorium purpureum, Hepatica triloba, Iris versicolor, Serpentaria, Panax quinquefolium, Symplocarpus fetidus.

The following plants at one time plentiful are now rare:

Apocynum cannabinum, Apocynum androsæmifolium, Arum triphyllum, Asarum canadense, Asclepias incarnata, Caulophyllum thalictroides, Ceanothus americanus, Celastrus scandens, Cimicifuga racemosa, Collinsonia canadensis, Euonymus atropurpureus, Eupatorium perfoliatum, Geranium maculatum, Gnaphalium polycephalum, Hydrangea arborescens, Hydrastis canadensis, Hypericum perforatum, Jeffersonia diphylla, Juglans cinerea, Lobelia inflata, Polemonium reptans, Polygala senega, Polygonatum biflorum, Pulmonaria officinalis, Sanguinaria canadensis, Scutelaria lateriflora, Senecio aureus, Tanacetum vulgare, Trillium erectum, Verbena hastata, Xanthoxylum americanum.

The following plants are locally frequent:

Dicentra cucularia, Dicentra canadensis, Chenopodium anthelminticum, Epigæa repens, Leonurus cardiaca, Marrubium vulgare, Mentha piperita, Mentha viridis, Oenothera biennis, Penthorum sedoides, Phytolacca decandra, Polygonum punctatum, Podophyllum peltatum, Rhus glabra, Scrophularia nodosa, Sambucus canadensis, Solanum carolinense, Verbascum thapsus.

The plants listed below are still found in commercial quantities:

Achillea millefolium, Capsella bursa-pastoris, Galium aparine, Hedeoma pulegioides, Lactuca virosa, Nepeta cataria, Plantago major, Rhus toxicodendron, Rubus strigosus, Rumex acetosella, Rumex crispus, Solidago odora, Taraxacum dens-leonis.

But one need not confine himself to the local flora in making a garden of herbs. I have used the following list to work from. Most of these plants will grow almost anywhere in the United States, provided the soil, sun, exposure, etc., are suitable. Some of them, as Gelsemium and Passiflora, which are marked "tender" are winter killed in the North. I have failed so far to get them to grow in Cincinnati, but still have hopes. And that is the keynote of the gardener's character. He is a born optimist. No matter what happens this year he has hopes for next year. The line "Man never is but always to be blest" must have been inspired by contemplation of a gardener.

Many of the plants listed by nursery men are used or have been used in medicine, and it is easy, therefore, to give a medicinal slant to your garden. The following list compiled from the catalog of Bobbink & Atkins of Rutherford, N. J., will offer suggestions to any one who may be tempted to undertake for himself a garden of herbs.

Name.	Height.	Flowering month.	Class.	Color.
Achillea millefolium	2′	7–9	2	White
Artemisia abrotanum	2–3′	7	2	Greenish
Asclepias tuberosa	2′	7–8	2	Orange
Papaver orientale	2′	6–7	2	
Spigelia marilandica	1½′	6–7	2	Red
Anthemis nobilis	2′	6–7	2	White
Marrubium vulgare	2′	7–8	2	White
Mentha piperita	2–3′	7–8	2	Purple
Mentha spicata	2–3′	7–8	2	Purple
Liatris spicata	2–3′	7–9	2	Purple
Lavandula officinalis	2′	6–7	2	Blue
Salvia officinalis	2′	6–7	2	Blue

Hyosopus officinalis			♃	
Ruta graveolens			♃	
Asclepius incarnata	3–4′	8	♃	Pink
Valeriana officinalis	3–5′	8	♃	Pink
Eupatorium urticafolium	4–5′	8	♃	White
Eryngium yuccafolium	3–4′	7	♃	Greenish white
Cimicifuga racemosa	4–5′	6–7	♃	White
Eupatorium purpureum	6–7′	7–8	♃	Purple
Cassia marilandica	5–6′	7–8	♃	Yellow
Aspidium filix mas	15″–15″			
Lilium tigrinum	2′	8–9	Annual	Orange
SPRING FLOWERS:				
Helleborus niger	9″–15″	3–4	♃	White
Hepatica tribloa	4″–6″	4–5	♃	Blue
Polemonium reptans	8″–12″	4–5	♃	Blue
Sanguinaria canadensis	6″	4–5	♃	White
Mertensia virginica	12″	5–6	♃	Rose
CREEPERS:				
Arctostaphylos uva ursi	2″–4″	4–5	♃	White
Epigaea repens	2″–4″	3–4	♃	Rose
CLIMBERS:				
Humulus lupulus		7–8	♃	Greenish
Euonymus atropurpureus		6–7	♃	Brown
Celastrus scandens		5–6	♃	Brown
Solanum dulcamara		6–7	♃	
Passiflora lutea		6–7	♃	
SHRUBS:				
Crataegus oxyacanthea	2′–3′	5–6		White
Hydrangea arborescens	3′–6′	7–8		White
Hamamelis virginiana	5′–8′	10–11		Yellow
Viburnum prunifolium	5′–8′	5–6		White
Viburnum opulus	5′–8′	5–6		White
Sambucus canadensis	5′–8′	6–7		White
Chionanthus virginiana	5′–8′	6–7		White
Ptelea trifoliata	5′–8′	6–7		
Cornus florida	5′–25′	5–6		White
Oxydendron arborus	5′–25′	6–7		White
Ceanothus americana	2′	6–7		White
Rhus canadensis	3′–8′	3–4		Yellow
Xanthorrhizza apiifolia	1′–2′	4–5		Brownish
Gillenia trifoliata	3′–4′	5–6		White
EVERGREENS:				
Juniperus communis	1′–2′			
Comptonia asplenifolia	1′–2′			
Prunus strolens	5′–150′			
Thuja occidentalis	5′–100′			
Thuja canadensis	5′–78′			

In addition to what I could find in the woods, I called on friends for assistance, and Dr. F. B. Kilmer, of Johnson and Johnson, New Brunswick, sent me a handsome collection of small belladonna plants and several second-year roots. Professor L. E. Sayre, of Kansas, sent me a supply of *Echinacea angustifolia*, Dr. W. W. Stockberger of the Bureau of Plant Industry sent *Iris versicolor*, which was at one time

quite plentiful in Hamilton County, but which is long since extinct, *Inula helenium*, and a dozen varieties of drug plant seeds. These sources have been supplemented by purchases from collectors in the North Carolina mountains, and from a nursery at Hopedale, Ill., which makes a specialty of drug plants, and from local sources, including fellow members of the Cincinnati Branch of the American Wild Flower Preservation Society.

The results so far are interesting though not very attractive from a strictly horticultural point of view; in fact, the average layman would be inclined to sneer at my collection as a "passel of weeds," but to the one who has been familiar with drug names and drug products all his life there is a keen fascination in watching the development of the plants from the seed or from the seedlings into the forms figured in the books and described in the Pharmacopœia and the National Formulary.

The soil, the location, and even the atmosphere of my garden are decidedly unfavorable, for the earth was originally building debris with a scant covering of tillable soil. The presence of smoke in the atmosphere (for there is still smoke in Cincinnati, even since the introduction of natural gas, though the conditions are very much improved), the tall buildings, surrounding the little plot, and the strong currents of wind which dry out the soil and tear off the leaves of the tender plants — all militate against our little garden of herbs. But in spite of all this the number of plants grow and as the soil improves with tillage and the constant addition of fertilizer, their size increases.

On account of the esthetic demands of the situation, for the garden occupies the front yard of the office, I have been compelled to introduce plants little if ever used in medicine, such as dahlias, gladioli, *lilium auratum*, etc., and for the Spring garden I have had to go quite outside of medicinal plants in order to get an adequate showing of color.

When I see what has been accomplished by Dr. Newcomb at the University of Minnesota, by Dr. Lyman at the University of Nebraska, and by others who have at their command the resources of a university and of an entire state, and who consider the growing of drugs as a vocation and not as an avocation, I feel almost ashamed to talk about our little garden of herbs. But to the pharmacist, even if he has limited means and restricted leisure, there is a possibility of great pleasure in the making of such a garden, and if he is fortunately located he will find that his trips to the woods in search of indigenous drug material will be the happiest and healthiest way in which he may spend his Sundays and holidays.

THE QUESTION OF SOIL.

Most of our drug plants are woods plants, and accustomed to an acid soil which is one reason why I have such a high plant mortality in my garden. Professor Coville and Dr. Wherry of the Bureau of Plant Industry have made some interesting studies of this phase of the subject and Bulletin No. 1 of the American Horticultural Society tells of the successful use of aluminum sulphate for rendering the soil acid where one wishes this condition to prevail. In a rough way about a half pound of aluminum sulphate is spread on each square yard of the soil, but the only safe way to render the soil acid is to keep adding the sulphate until the soil gets the acid reaction. Of course, there are many plants which require an alkaline

soil. This opens up a very interesting field for study and observation. For instance, we cannot grow any of the ericaceae, rhododendrons, azalias, etc., in Cincinnati, on account of the alkalinity of the soil. I hope to be able to do this by the aid of aluminum sulphate.

BEZOAR.*

BY WILLIAM KIRKBY.

The *Via Appia* of historical medicine presents to the eye of the traveller many tombs of dead theories and of defunct remedies, some of which may repay a half hour's contemplation by the student of anthropology. Even in these later times of high scientific attainment it is a quite common experience to find people, under the compulsion of bodily pain or mental distress, indulging themselves in the hope, and often in the belief, that a panacea will be forthcoming for each and every ill that flesh is heir to. Such a hope may be vain, but if it keeps alive the spirit of research, as we believe it does, it is by no means unfruitful. In the quest of agents to alleviate human suffering it is natural that the keener vision, which enlarged knowledge supplies, should often be directed backwards over the travelled path to see if each by-way has indeed been thoroughly explored. Thus it comes to pass that old remedies are resuscitated and tried again in new circumstances and in new combinations. Indeed it is in but a few cases that we can feel assured that an expired remedy is really beyond the call to a resurrection. Of these few there is one which is sufficiently interesting, I think, to occupy your thoughts for a few minutes because its vogue was at its height for a fairly well-defined period, because it is a good illustration of the deep-seated desire to possess a panacea, because it exhibits a prevalent human weakness to cherish the notion that the mysterious may, and probably does, achieve results of a miraculous nature, and because when the character and composition of the remedy were tested in the true scientific spirit it was manifest that its supposed medicinal properties were nonexistent and would not sustain the belief in its reputed virtues of the most credulous civilized person.

Bezoar stones are now merely medical curiosities, but during the seventeenth century and part of the eighteenth they were highly valued as a medicine of great efficacy. In 1621 we find Robert Burton writing in "The Anatomy of Melancholy," in the subsection in which he discourses on "Alteratives and Cordials," that

> "Christophorus Ayrerus prefers Bezoar stone and the confection of alkermes before other cordials, and amber in some cases. Alkermes comforts the inner parts, and bezoar stone hath an especial virtue against all melancholy affections; it refresheth the heart and corroborates the whole body. . . . . After a purge three or four grains of bezoar stone, and three grains of ambergrease, drunk or taken in borage or bugloss water, in which gold hot hath been quenched will do much good."

He goes on to say that

> "To bezoar stone most subscribe, Manardus and many others; 'it takes away sadness and makes him merry that useth it; I have seen some that have been much diseased with faintness, swooning and melancholy that taking the weight of three grains of this stone, in the water of oxtongue, have been cured.' Garcias ab Horto brags how many desperate cures he hath done upon melancholy men by this alone, when all physicians had forsaken them."

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* Section on Historical Pharmacy, A. Ph. A., Cleveland meeting, 1922.

On the other hand that most sceptical physician, "whose whole life was 'wrapt in a pure flame and ecstasy of high curiosity' "—Sir Thomas Browne—was not imposed upon by the great praises lavished upon bezoar.[1]

It is said that Avenzoar was the first to introduce this remedy. Avenzoar was an Arab physician who was born in Seville in the eleventh century and is said to have lived to the age of 135 years. He practiced in his native city, and, according to the best authorities, he died in Morocco about 1217. Bezoar was recommended by him as an antidote for jaundice which he imagined to be the effect of poison. His account of the origin of the drug is curious. He says:

"The best (Bezoar) is found in the East, where it is produced from the eyes of the Deer. In those countries the larger kinds of deer eat serpents for the purpose of improving their strength and, before they have sustained any injury from them, they run down to the rivers, and plunge themselves in water up to the head, a practice taught them by instinct; here they remain immersed, without drinking (which would be instantly fatal) till their eyes begin to water; this humour continues to exude under their eyelids, and coagulates there till it acquires the size of a chestnut. As soon as the deer find the venom of the serpent exhausted, they quit the water, and return to their usual haunts, when the concretion, hardening progressively to the consistence of stone, drops off at length by frequent friction."[2]

There are other early references to Bezoar in the works of the Arabian physicians, but they are of a vague character and in not a few instances the references are not so much in regard to the drug as to the word Bezoar which was used apparently as signifying alexipharmacal. By the beginning of the seventeenth century a considerable amount of information, of a more or less authentic nature, concerning Bezoar and bezoardic drugs was available and was collected by Caspar Bauhin in his *De Lapidis Bezaaris* (1625). This treatise is divided into fifty-two chapters and the author has drawn on the writings of no less than one hundred and eighty-five authorities. As a further indication of the thorough researches of Bauhin as well as of the widespread interest in bezoardic remedies it is worth pointing out that in the first chapter—*De Nomine Bezaar*—his references reach the high figure of sixty-nine. I do not propose to take you through this most interesting volume which, as you will gather, contains pretty well all that was known of these substances at that time.

The derivation of the name indicates the use of the drug. Bezoar, according to almost all the authorities, ancient and modern, is derived from the Arabic—*bāzahr* or *bādizahr*, Persian—*pādzahr*, meaning an antidote or counterpoison.[3] In the older literature the word assumed a great variety of forms. Bauhin mentions Bedazahar, Albezahar, Bezahar, Bezarad, Bedezarahath, Bezahart, Bezachar, Bedzahar, Bezaar, Bezadaret, Berzad and others. An old English dictionary[4] gives an origin for the word which differs from any other I have met with: "Bezoar, from the Persick *Pazar* or *Pazan*, a Goat, because it is found in the Belly of a certain Goat." Bauhin in giving the Hebrew name, Belzaar, says that it is a compound of *Bel* and *Zaar* signifying "the Master or Overcomer of Poison."

As to the virtues of the substance there is much evidence to show that it was regarded as a general antidote when administered internally, and it was thought

[1] *Pseudodoxia Epidemica*, 1646.

[2] Wm. Hamilton, "History of Medicine," Vol. I, p. 267, 1831.

[3] Murray & Bradley's "Oxford English Dictionary."

[4] *Gazophylacium Anglicanum*, 1689.

that it possessed magical properties and, in consequence, it was worn as a charm or amulet. Matthiolus[1] says that its special virtue is that it is a most excellent remedy against poisons in general; it is, he continues, not only taken internally, but is also worn on the person in such a way as to touch the naked flesh on the left side, and when so worn it overcomes all poisons. In his "*De Simplicium Medicamentorum*" he writes of *Lapis Bezahar* as an antidote to all poisons whether communicated by bite or a blow; twelve grains may be given in a draught and the drug should be smeared on the wound. He also recommends it specifically for the bite of the viper and as an antidote against aconite poisoning when seven grains should be given in pure white wine (*Septem grana ex albo meraco*).

Having seen how the name and reputed virtues of Bezoar have reacted upon each other we may now enquire what was the origin of the drug as recorded by those writers who sought a reasonable account of it, in place of such traditional stories as that we have already referred to.

In the seventeenth and eighteenth centuries we have descriptions given of several kinds of Bezoar, of which the chief varieties were *Lapis Bezoar Orientale* and *Lapis Bezoar Occidentale*. Bauhin's monograph was the work from which subsequent writers took the statements which, by degrees, with the increase of knowledge, gradually became qualified and modified so as to more nearly represent the actual truth. Schroeder[2] says that Bezoar stone of the East is found in

> "a Persian or East-Indian Beast, partly like a Deer, partly like a Goat, called the Indian Goat, or Deer-like Goat—chiefly in the stomach and other cavities within, of an oval form, or round and hollow within (having chaff or hair, or the like within it), shining and smooth without, with folds like an onion, of a divers colour, commonly of a blackish green, or clearer green, or pale, or Ash-coloured, or Honey-coloured, with no scent: of a different bigness and weight, they being less than Walnuts, sometimes bigger."

The *Lapis Bezoar Occidentale* he says is obtained

> "from a Beast of Peru, like the other of the East, but without Horns, that eats wholesome Herbs." The stone is "without any strange thing in the cavity, with coats, bigger commonly than the Eastern, rough without, Ash-coloured, white or black, or blackish green which is best."

Lovell's[3] description is similar to the foregoing, and his account of the origin of the stones is taken from Bauhin's work to which he refers his readers. Pomet[4] in 1694 gave a long account of *Bezoar orientale* and *occidentale* as well as of other varieties of Bezoar from other countries and other animals. His volume, as you are aware, is well illustrated and among his pictures is a curious one of the "Bezoar Goat" with horns which are quite unlike the horn figured by Bauhin. Pomet's article contains a large amount of matter derived from Tavernier, De Renou[5] and Lemery.[6] Another writer of the seventeenth century, William Salmon,[7]

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[1] *Commentaires de M. Pierre Andre Matthiole sur les six livres de Ped. Dioscoride*, Lyons, 1572.

[2] "The Compleat Chymical Dispensatory," by John Schroeder, Englished by William Rowland, 1669.

[3] *Panzoölogicomineralogia*, by Robert Lovell, 1661.

[4] *Histoire generale des Drogues par P. Promet*, 1694. English translation, 2nd Edition, 1725.

[5] "Medicinal Dispensatory," Englished, 1657.

[6] *Dictionaire des drogues simples.*

[7] "The Compleat English Physician," 1693. "The New London Dispensatory," 1678.

gives a compendious summary of all that had been previously written concerning the origin, characters and virtues of Bezoar and mentions most of the better known authorities on the drug.

Bezoar stones were held in very high esteem, as were indeed almost all kinds of remedies obtained from animals. The more difficult conditions attaching to the obtaining of a drug inspired the more abundant faith in it as a panacea for some sickness or other. I should think it is most unlikely for one to meet with a Pharmacopœia or Dispensatory published in the seventeenth century which does not include *Lapis Bezoar* and one or more preparations of it. It was made official in the first *Pharmacopœia Londinensis* (1618) and continued until the 1746 edition after which it was deleted. The insolubility of Bezoar led to its being exhibited generally in only two classes of preparations, namely, confections or electuaries, and powders. Bauhin gives a formula for "*Antidotus Bezaartica adversus omnia venena*"[1] which contains over forty ingredients including the true Oriental Bezoar, gold leaves, prepared emeralds, Mithridate, and the *Theriaca Andromachi;* the two latter preparations represent more than another hundred ingredients. Perhaps one may be excused for quoting a formula not quite so elaborate but which will serve to illustrate the kind of preparation in which Bezoar frequently found a place. It is taken from the *Pharmacopoea Dogmaticorum Restitua* of Quercetanus (1614):[2]

Antidotus minor contra pestem.
R. Succi Scordii
Rutae
Cardui benedicti
Ulmariae
Menthae crispae
Salviae ana unc. 4 vel plus minus.
Rad. Angelicae
Zedoariae ana unc. 1.
Dictamni
Sem. Cardui benedicti
Cort. Citrii ana unc. sem.
Cinnamomi drach. 6.
Myrrhae unc. 2.
Croci drach. 3.
Camphorae drach 1.
Theriacae optimae unc. 1. sem.
Confect. Hyacinthi.
et Alkermes ana unc. 1.
Perlarum praeparatorum
Corallor. praeparatorum
Cornu Cervi praeparati
Spec. Diambrae
De gemmis ana drach. 2.
Unicornu drach. sem.
Lapidis bezoardici drach. 1.

This work of Quercetanus requires that it should be mentioned here that in it he refers to a *Bezoar metallicum fixum* and to bezoardic preparations which contain no Bezoar stone. For one of these latter he gives a formula the ingredients of which are principally what we should class as carminatives; it is named *Praeparatio extracti bezoardici.* This volume was not overlooked by Bauhin. Without attempting to give you any adequate notion of the extent of the use of this drug by naming the many authorities with which I have become acquainted I may content myself with referring to De Spina's *Lexicon Pharmaceutico-Chymicum*[3] in which there are three formulae for *Pulvis Alexipharmacus* each containing *Lapis Bezoar,* and twenty-five formulas for *Pulvis Bezoardicus* attributed to as many different authorities. The esteem in which it was held was truly extraordinary.

[1] *Loc. cit.*
[2] The first edition appeared in 1603.
[3] 2nd Edition, 1715.

Lovell[1] in his monograph has between five and six pages dealing with the uses of the drug and the authors whose works had been consulted. There is other evidence of a more striking kind testifying to its tangible value. Matthiolus[2] says, on the authority of Abdalanarakus, that a magnificent palace at Cordova was bartered in exchange for one of these Bezoar stones. Bauhin[3] gives instances of monetary value and tells of one stone which was sold for one hundred and thirty gold ducats. Pomet[4] states that an ounce was worth from fifteen to twenty *livres* (francs), but a single stone of that weight would sell for a hundred *livres*. He, himself, sold one weighing four and a quarter ounces for two thousand *livres*. Salmon[5] giving his experience writes:

"now they are much more plentiful; the best Oriental green ones have borne price from 30 shillings to 50 shillings an ounce, but of late (by reason of the plenty of Occidental ones) they have been sold much cheaper, scarcely reaching 20 shillings an ounce. The Occidental are worth from 5 shillings to 12 shillings an ounce."

This exaggerated idea of the value of Bezoar was not entertained by everyone. Boyle,[6] for instance, states:

"That the Bezoar stone, sold at an immense price, is in every way inferior in virtue to the *Calculus Humanus*, we have the testimony of the experienced Bontius."

Pitt in 1702 published his "*The Craft and Frauds of Physic Expos'd*" and in it makes use of the Bezoar stone as an illustration of the credulity of the physicians of his day. Some quotations will serve to show that scepticism of its value was by no means confined to a few. He affirms that "Bezoar has held its Name and Reputation almost Sacred with us, tho' exploded long since in almost all the Parts of Europe. Dr. Guybert in a Discourse entitled '*Les Tromperies du Bezoar decouvertes, The Cheat of Bezoar laid open*,' convinced the French that they had been imposed on by the Trading Physicians returning from the Indies." He tells of the "Two Criminals who by the King's Command had poyson given them with the promise of Life if Bezoar could procure their Pardon. They lost their lives and the stone and the Physicians their Reputation."

He gives an imposing list of names from Guibert's treatise of those who do not believe in the drug. Among them are Diemerbroeck, Paré, Sennert, Sanctorius, Mindererus, Rulandus, Bauhin, Hoffmann, and Bontius who tells us

"That if we must give stones we ought to put a greater value upon the Stones cut out of the Bladders of Man, a more noble creature, fed with meat of the highest nourishment and his Spirits warmed with wine, than that of a Goat, starving upon the Mountains."

Up to this period the history of this substance has been an account of specific superstition, credulity and gullibility, on the one hand, and of scepticism, assertion and, sometimes, prejudice on the other hand. We have heard practically nothing of any attempt to estimate the medicinal value of it when exhibited alone—as distinct from the theatrical episode of using as an antidote to a virulent poison.

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[1] *Loc. cit.*

[2] *Loc. cit.*

[3] *Loc. cit.*

[4] *Loc. cit.*

[5] *Loc. cit.*

[6] "The Usefulness of Philosophy," published 1671, in Peter Shaw's 2nd Edition of "The Philosophical Works of the Honourable Robert Boyle," 1728, Vol. I.

The history of many other drugs is of a similar character, but in this case the exaggerated reputation of the substance inspired not only the jealous prejudices of some physicians but it brought into play the spirit of research of a man whose name is not very familiar in the annals of medicine. As has already been intimated Bezoar stones were administered for the most part in the powdered form in electuaries and compound powders. They were used as amulets attached to gold and silver frames and chains for hanging about the person of the patient, and, although practically insoluble in wine and water, they communicated a bitter taste to the liquid in which they were placed, and the infusion was thought to be efficacious in many ailments. Being so valuable the stones used in this way were attached to gold chains and preserved in gold boxes. Some of these specimens are said to be found in museums but it has not been my good fortune to meet with any. Dr. Frederick Slare was a man, as he himself indicates, well versed in the knowledge of the Materia Medica and interested in the nature and properties of the medicines in common use which he was led to examine and was well acquainted with the facts just mentioned. Bezoar being as Slare says "of the first Rank" it became very early the subject of his "Test and Scrutiny" and he soon found that "it did not deserve the great Encomiums which were given it." The results of Slare's examination were read before the Royal Society, of which he was a Fellow,[1] and were published in 1715.[2] This is a record of twenty years' work which "required both Expense, Patience and Industry, accompanied with some Sincerity and Honesty." I don't propose to follow Slare through the record of his enquiries in the course of which he tested Bezoar stones as to their solubility in different fluids and as to the clinical value of the drug when exhibited alone. Bezoar was one of the chief constituents of the so-called "Gascoign's powder." Slare also submitted this preparation to his scrutiny. His final conclusion was that chalk is a more useful remedy than either Gascoign's powder or Bezoar—"But" he continues "it must be confessed that this useful Salt lies under the vile Reproach of being cheap, compared with those enriching Powders we have examined." In his correspondence with his friends in the East he elicited the fact that only about one goat in seven was found to yield a stone. Twelve stones on the average weighed an ounce. It was not difficult to compute what number of goats would require to be killed to supply one druggist. A druggist, a particular friend of his, told him he used five hundred ounces a year. So that over 40,000 goats would have to be killed to supply one establishment. It is small wonder that genuine stones were very rare and difficult to obtain, and that the great majority were counterfeit.

Notwithstanding Slare's work Bezoar continued to be regarded as a remedy of importance for many years. Every dispensatory and compendium of medicines gave it and its preparations the fullest notice; but the London Pharmacopœia of 1746 was the last one in which it was official. Having reached this period it seems that we may look at the collected information which was brought together by James in the first volume of his "Medicinal Dictionary," published in 1743.

[1] Slare was a man of marked ability. He has been well described as "a forerunner of the almost exclusively clinical school of Sydenham." But he was also a chemist; he demonstrated the presence of sodium chloride in the blood, and in Evelyn's diary we have an account of him showing experiments with phosphorus at the house of Samuel Pepys.

[2] *Experiments and Observations upon Oriental and Other Bezoar-Stones Which Prove Them to Be of No Use in Physick*, by Frederick Slare, 1715.

He devotes about four folio pages to it. He says it is nothing but a stone formed in the gall bladder of several species of animals found in the East and West Indies such as goats, hogs, apes, etc. It is also sometimes found in other parts of these animals. From James' account of his examinations of Bezoar stones it appears fairly certain that the stomach and intestines are the organs in which the stones are found, because there are many in which is found a nucleus of some ingested foreign substance. They are laminated and in form may be round, oblong or reniform. The consistence is firm and the surface generally smooth. Water and spirit of wine are rendered turbid when a Bezoar stone is placed in them, but no appreciable quantity is dissolved. The evidence adduced by this author is not at all conclusive as to the organic origin of the stones. Neumann[1] is no more illuminating. He quotes Kaempfer: "that the genuine Bezoar is in Persia itself so rare and so dear, that he cannot believe that a single stone comes into Europe." Neumann continues: "Many others agree in this account; and indeed the Bezoar stone carries in itself strong marks of art, but hardly any traces of its being formed by nature." It is not surprising, therefore, that Neumann's experiments do not result in any certain indication as to how and where the stones are formed. Perhaps it would have been as well if I had followed Wm. Lewis in his method of treating the subject, but you will apprehend that my discursive treatment is for another purpose than merely conveying predigested information. In his "Experimental History of the Materia Medica"[2] he states that the "Oriental Bezoar stone is supposed to be produced in the pylorus, or in a cavity at the bottom of the fourth stomach, of an animal of the goat kind." "Occidental Bezoar: said to be found in the stomach of an animal of the stag kind." "*Lapis Simiae*—Bezoar of the monkey: said to be found in the stomach of certain monkeys." "*Calculus humani, bezoar microcosmicum quibusdam dictus*—The Calculus of the human bladder." "*Lapis Porcinus—Bezoar Hystricis:* Bezoar of the porcupine: said to be found in the gall-bladder of an Indian porcupine." This writer commits himself to a definite statement only in the case of the *calculus humani;* the other statements are founded only on "hear-say."

The brief history of Bezoar serves to illustrate again the small amount of reliance to be placed upon the reports of merchants and travellers. Slare tells of two most trustworthy friends in the East who had to confess they had been misled in the accounts which had been given them concerning the obtaining of the stones. It is only when we reach a period in which actual scientific investigation has been brought to bear on the matter that we obtain any certainty at all. Fourcroy, Vauquelin and Berthollet examined a number of animal concretions and they placed them in eight classes. These researches threw much light on the problem. Berthollet found that the three Bezoar stones sent by the Shah of Persia as a royal gift to Napoleon Bonaparte consisted only of agglomerated woody fiber and were probably produced in the stomach of some animal in the same manner as the so-called hair-balls. Authentic intestinal calculi from herbivorous animals consist of concentric layers of ammonium-magnesium phosphate with a nucleus of plant residues. More recently, what were considered to be two different varieties of Bezoar stones have been chemically examined: (*a*) of an olive-green color, faintly shining and formed of concentric layers which yielded as its chief constituent

[1] "Chemical Works," abridged by Wm. Lewis, 1759.

[2] 2nd Edition, 1768.

lithofellic acid ($C_{20}H_{36}O_4$) together with some lithobilic acid, while (*b*) had as its principal constituent ellagic acid ($C_{14}H_6O_8$).[1] We may conclude, therefore, that Bezoar stones have an intestinal origin. The Persian, or so-called *Bezoar orientale*, being obtained from the *Capra aegagrus* (Capra hircus aegagrus) and the South American, or so-called *Bezoar occidentale*, from the South American Deer, *Mazama bezoartica* (?).

In the Museum of the Pharmaceutical Society of Great Britain there are two specimens of *Bezoar orientale* of which one is cylindrical and oval at the ends, it is two and a half inches long and an inch in diameter; the other specimen is kidney-shaped and is $1^3/_4$ inches long and $1^1/_4$ inches in diameter. Both are laminated, have a dark greenish color and have a polished surface. There are several of these stones in the Wellcome Historical Medical Museum and through the kindness of the Curator Mr. C. J. S. Thompson, M.B.E., I am able to show you photographs of four of them. No. 1 weighs four drachms, and in color is speckled gray and white; No. 2 weighs one drachm, No. 3 thirty-five grains and No. 4 seventeen grains. The three latter are all brownish gray in color.

Courtesy of the Wellcome Historical Museum, London

1 2 3 4

I should have liked to say something about the *Bezoar animale*, *Bezoar minerale* and the so-called Bezoars of metallic origin but these must find a place, perhaps, in another communication. I think I may appropriately close this paper with a reflection made by that eminent teacher of Materia Medica, Anthony Todd Thomson, when writing on Bezoar stones to the effect that they "afford an addition to the many thousand proofs of the influence of mind over the body, and show how truly efficacious Imagination may prove in removing disease."[2]

I must take this opportunity of expressing my sincere thanks to Mr. Thompson of the Wellcome Historical Medical Museum for his courtesy and kindness in providing me with photographs for this paper.

[1] O. Hammarsten, "Text Book of Physiological Chemistry," 3d Edition, 1901. Schmidt and Langlebert (*Repertorie de Pharmacie*, July 1886; through *Pharm. Journal*, July 31, 1886) report that they examined a South American specimen said to be obtained from the intestines of the *Antilope rupicapra*, which consisted chiefly of calcium oxalate. This appears to be a quite unusual constituent.

[2] Eusebe Salverte, "The Philosophy of Magic," translated by Anthony Todd Thomson, M.D., 1846.

THE BUSINESS SIDE OF PHARMACY

This department is devoted to the discussion of problems of business administration and commercial policies relating to the various branches of pharmacy.

CONDUCTED BY DR. ROBERT P. FISCHELIS.*

The Domestic Commerce Division of the U. S. Bureau of Foreign and Domestic Commerce recently held a conference in Washington with representatives of five associations of retailers including grocers, dry goods merchants, clothiers, shoe dealers and hardware men. The object of the conference was not to discuss the individual problems of any member of this group, but, rather, the fundamentals of retailing. That is why the conference should have been of interest to druggists and one is apt to wonder why they were not represented.

It is very interesting to note briefly the trend of the discussions and the splendid analysis of the function of the retailer which was presented at this conference. In the first place the function of the retailer was defined as follows:

"The retailer performs the final function in distribution of essential commodities and gives fulfilment to all preceding efforts by making merchandise available to consumers at the time, place, and in the form required by them.

"The retailer's true function is that of serving as a purchasing agent for his community; as such he selects and carries a reserve supply of merchandise to meet the requirements of the individual consumer.

"When the retailer enters business he assumes the responsibility of performing a public function, that of providing commodities and services to his community, economically and conveniently, and maintaining such environment as is necessary and desirable to the consumers who support him. If he fails in his responsibility and performs only as a distributing agent for the manufacturer, he ceases to be an economic factor in the community which he serves."

If we add to the above such statements as would adequately describe the particular professional service which the pharmacist performs, we would have as fine a description as anyone might desire of the true function of a retail druggist and one that the highest type of professional man could find no objection to.

It was brought out in the conference that the retailer in his relation to the public has a double duty to perform. He must act as a purchasing agent and he must render a selling service.

As a purchasing agent for the consumer he must possess capital and credit. He must have a knowledge of raw materials and finished products. A knowledge of market resources and commercial conditions is also essential. He must know how to obtain prompt deliveries and attend to the proper receiving, arranging and marking of goods. A knowledge of turnover is necessary. Stock must be reordered with sufficient frequency and a minimum of expense. A knowledge of the uses and purposes of all commodities sold is essential as is also a knowledge of style, the best buying seasons and the best methods of buying. It is important to be able to use trade association facilities to the greatest advantage. A knowledge of the requirements of consumers in the community is of course at the very basis of successful retailing. Such knowledge requires constant study of the demands of a community and study of new requirements resulting from changing economic conditions.

Proper sales service to the public involves maintaining an adequate stock of merchandise of quality and value to meet the requirements of the community;

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maintaining facilities and environment to economically and efficiently serve the requirements of a community; assuming responsibility for merchandise distributed; selecting, educating and stimulating the sales force; providing proper publicity through newspapers, circulars, direct mail and telephone as well as by means of window displays and demonstrations.

The conference gave recognition to the fact that the retailer, the wholesaler and the manufacturer each has his separate function, and that upon the efficiency with which each performs his functions depends the economy of distribution. A clear definition of functions and the elimination of overlapping and duplication of activities offers a source of immediate economies.

Stock turn is recognized as one of the basic factors in economical distribution. Store departmental studies of distribution offer a basis for the determination of the most effective means of increasing stock turn and reducing retail operating expense.

Future buying too far in advance is one of the outstanding problems of retailing and contributes in large measure in many lines to increased operating costs. In its effect it adds to the problems of the wholesaler and manufacturer. In the latter case it contributes to the cost of distribution and is reflected in operating costs of manufacturing.

A factor which contributes in no small measure to operating costs of retailing in certain lines, results from certain expectations of the public in the matter of extravagant and uneconomical rate of return of goods, a situation to which the retailer himself has to some degree contributed in the competitive effort to attract trade.

The Domestic Commerce Division was commended for its practical approach to the problems of domestic commerce through an analysis of factors involved in distribution, and its purposes of establishing a basis of fundamental principles as a means of correlating distributive effort from the producer to the consumer.

An extract from a formal statement issued by the conference before adjournment is of interest and is printed below. With such effective coöperative work going on among retail organizations with the assistance of the government it seems as though better business methods must result. The business side of pharmacy can profit immensely by keeping in touch with these developments—or better still, by taking part in them.

"It is the judgment of the conference that the Department of Commerce can materially assist retailers to render the most efficient service by directing studies in the entire field of domestic commerce, with the object of improving practices, determining justifiable costs and eliminating wastes.

"The conference assures to the Department of Commerce the full support of the organized retail associations represented and promises their coöperation in such further studies as the Department of Commerce may undertake."

"The conference of representative retail trade associations recognizes the value of an exchange of views and of a presentation of the specific problems inherent in their several branches of retailing, and expresses great satisfaction in the fact that a disinterested branch of the Government, like the Department of Commerce, has undertaken a study of the facts of retailing.

"The conference expresses the hope that the Department of Commerce will undertake not only to educate and inform the public as to the facts of distribution, but that it will assist in the dissemination of knowledge to the men who are them-

selves engaged in retailing concerning problems of distribution, not only in their own retailing spheres, but in the producing and manufacturing field as well, and that the Department will gather, correlate and compile the facts and figures of distribution, and that it will give the results such practical analysis, interpretation and publicity as will best serve the interests of the consumer, producer and distributor alike."

PROFIT, TOTAL SALES AND RENT.

BY J. A. W. LUCK.

Profit is customarily computed from the selling price of merchandise. It is therefore important to know the relation which exists between the percentage profit of the selling price and the percentage profit of the cost price. Strictly speaking, it is immaterial what manner is used to compute the profit, so long as a uniform method is used throughout all calculations. Butler Brothers in their "Way System Book" give tables, which show the amount that must be added to the cost price to yield a given percentage of the selling price. A very convenient method is the graphical representation of these two quantities. By establishing a mathematical relation between the two percentages an equation is formed which may be plotted upon squared paper. The accuracy will depend merely upon the scale of the plot.

Let A = Purchasing Price a = Percentage Profit of P. P.
B = Selling Price b = Percentage Profit of S. P.
u = Gross Profit

then $Aa = 100\,u$, and $Bb = 100\,u$, also $A = B - u$

therefore $Bb = Aa$ or $B = Aa/b$ (1)

$b = 100\,u/B$ (2)

$a = 100\,u/(B-u)$ (3)

In Figure 1, Curve A represents Fquation 2, percentage as ordinate and gross profit as abscissa. Curve B represents Equation 3 showing the relation as in Curve A. Curve C shows the relation b as ordinate to a/b as abscissa. In all three cases B is taken as unity.

TABLE I.

a.	b.	u.	a/b.
0	0	0	1
1.01	1	0.01	1.01
11.11	10	0.1	1.11
25	20	0.2	1.25
66.66	40	0.4	1.66
100	50	0.5	2
150	60	0.6	2.5
400	80	0.8	5
900	90	0.9	10
9900	99	0.99	100
∞	100	1	∞

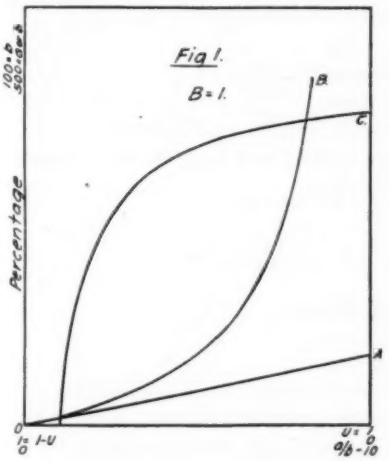
When b = 100, A must be equal to zero. The merchandise has been received gratis. It is to be noted that any value B for such merchandise will be equivalent to a gross profit of a 100%.

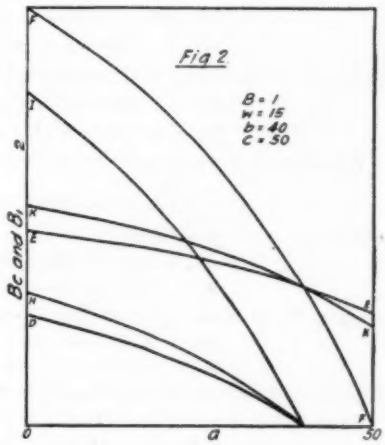
Equation 1 is the most important one, particularly if it is used in conjunction with Curve C. If we consider the purchasing price A = 1, then B = a/b. The

abscissa of curve C, therefore, represents values of B. Consequently, for any value of A, it is necessary only to multiply the value a/b obtained from Curve C for any value of b by A to obtain the value of B.

Frequently merchants are compelled to lower prices of their merchandise, usually due to competition, but also due to the desire to attract new customers to the establishment. However, few stores are so located that price cutting will bring them additional trade; to the bulk of the trade the result is a loss of part of the total receipts, gross profit and a consequent reduction of the net profit. Unless favorable conditions prevail, price cutting cannot be carried on very long because the net profit is lowered more rapidly than the gross profit. A method to overcome a loss of this kind is to introduce new merchandise which will yield a large return.

In order to have a clear conception of the profit of a business, a knowledge of the kind of merchandise sold is very necessary. The profit which is realized must be distributed properly, a loss in one case must be offset by a proportionately larger gain on some other articles.





For the proper adjustment of selling prices a system must be established and maintained. Unfortunately, the sales slip, which is one of the best methods to keep track of the individual articles, is not used to any large extent in the drug business. It is therefore necessary to divide the merchandise into profitable and unprofitable departments, using separate registers or a single register capable of registering departmental sales.

Such a system properly used will detect a decrease in the profit immediately. This loss can be easily checked by selling additional profitable merchandise. The amount of this new merchandise can be readily calculated in the following manner.

1. Gross Profit Constant.

B = original total sales	b = original gross % profit
B_a = reduced total sales	a = reduced gross % profit
A_c = cost of new goods	S = loss of gross profit
B_c = selling price of A_c	c = gross % profit of B_c
B_1 = new total sales	b_1 = new gross % profit

$$B - bB/100 + aB_a/100 = B_a$$

Therefore $B_a = B(100-b)/(100-a)$ (4)

Loss of gross profit $= bB/100 - aB_a/100 = cB_c/100 = S$

Therefore $B_c = 100B(b-a)/c(100-a)$ (5)

Also $A_c = B_c(100-c)/100$

and since $B_1 = B_a + B_c$

$B_1 = B[100(b-a) + c(100-b)]/c(100-a)$ (6)

In Figure 2 Equation 5 is represented by the Curve D, and Equation 6 by the Curve E. It is readily seen that as B_1 increases additional help may be needed to take care of this increase. Naturally, this will result in the reduction of the net profit. A better policy is to consider this problem by keeping the net profit constant.

2. Net Profit Constant.

Let w = % of the total sales necessary to pay wages. For convenience, we may separate the gross profit into four items, namely, net profit, wages, rent, and a value which we will call the index figure and represent it by the letter I. This index figure varies with each establishment and depends upon the capital investment and the overhead other than wages and rent. We may express this by the equation $bB/100 = I + r + W + P$.

P = net profit W = wages

I = index figure r = rent

For convenience we will write $I + r = O$.

$bB/100 - wB/100 = O + P = b_1B_1/100 - wB_1/100$

$b_1B_1 = bB - wB + wB_1 = aB_a + cB_c$

combining these equations with equation 4 and eliminating B_a,

$B_c = B(100-w)(b-a)/(100-a)(c-w)$ (7)

and $B_1 = B[(100-w)(b-a) + (100-b)(c-w)]/(c-w)(100-a)$ (8)

Equation 7 is represented by Curve H in Figure 2, and Curve K is the plot of Equation 8.

3. Per cent. Gross Profit Constant.

Therefore $b = b_1$ and

$aB_a + cB_c = (B_a + B_c)b = bB_1$

$B_a = B_c(c-b)(b-a)$

Eliminating B_2 by means of Equation 4 we obtain the relations

$B_c = B(100-b)(b-a)/(100-a)(c-b)$ (9)

and $B_1 = B(100-b)(c-a)/(100-a)(c-b)$ (10)

The Equations 9 and 10 are represented in Figure 2 by the Curves I and F, respectively.

In case 3 it was assumed that the overhead expenses remain constant. Should this not be the case, because either rent or wages or both are increased, the percentage gross profit may be increased to offset this change. An interesting study is case 1 when no attempt is made to sell additional profitable merchandise. We therefore have the condition that $B_1 =$, is greater or less than B. Consequently $bB/100 = O + pB/100 + wB/100$

where p = percentage net profit w = percentage wages

$B(b-w-p)/100 = 0$

Also $b_1B_1/100 = O + p_1B_1/100 + wB_1/100$

where p_1 = the new net percentage profit

Therefore $B(b-w-p) = B_1(b_1-w-p_1)$

or $p_1 = b_1-w-(b-w-p)B/B_1$ (11)

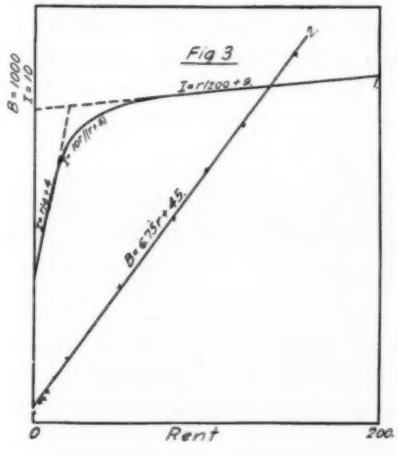
and $p_1B_1/100 = P_1$ (12)

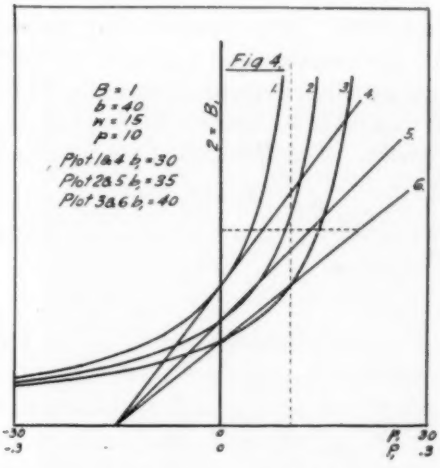
If we take B as unity, p_1 will show the percentage profit for any value B_1 at a fixed value b_1. This may also be stated as follows: p_1 is the net percentage profit when the total sales and the gross percentage profit are represented by B_1 and b_1, respectively.

The graphic representation of Equations 11 and 12 are shown in Figure 4. The hyperbolic Curves 1, 2 and 3 are obtained by plotting p_1 against B_1, when b_1 is equal to 30, 35 and 40%, respectively. These curves show at a glance the amount of total sales a business must have to yield a fixed net percentage profit if the gross profit is changed or the reverse. To obtain a net profit of 10%, Curve 3 gives the

value $B_1 = 1$, Curve 2 the value $B_1 = 1.5$ and Curve 1 the value $B_1 = 3$. Unless fortunate circumstances intervene such increases are difficult to attain, since already strenuous efforts must be made to obtain total sales equivalent to the rentals of to-day.

The straight lines 4, 5 and 6 are obtained by plotting values of P_1 against the corresponding values of B_1. Therefore, these lines show the net profit obtainable from increased sales at the same or different percentage gross profit. For a net profit $P_1 = 0.1$, line 6 shows $B_1 = 1$, line 5 shows $B_1 = 1.25$ and line 4 shows $B_1 = 1.666\ldots$ There is a further use of this plot, if a straight line is drawn parallel to the abscissa for any value of B_1, the line will intercept the curve and its corresponding straight line at points which represent the percentage net profit and net profit, respectively.





In general it will be found that case 3 presents the most profitable method to follow of the cases outlined above.

In determining the total sales necessary to gain a certain net profit at a fixed rental it is advantageous to make use of the index figure. As previously stated, the index figure includes all expenditure charged to the overhead account with the exception of the disbursements for wages and rent. It is important to include a charge for depreciation in this figure. "Butler Bros." suggest to write off each year, for three successive years, 25% of the value of the fixtures and then carry them on the books at 25%. In determining the proper relation for the index figure we have assumed a depreciation charge of 10% per annum.

The index figure is a variable quantity, and an exact figure for each drugstore can only be determined from the records of the store. Nevertheless, we can arrive at an approximate value by comparing the index figure with the daily rental of each establishment. By comparing a large number of data it is found that for small values of r, r and I are related to each other in the manner represented by the equation

$$I = r/4 + 4 \qquad (13)$$

For daily rentals between $6 and $90, I and r may be represented by the hyperbolic equation

$$I = 10r/(r + 5) \qquad (14)$$

Above $90 the available data are very meager and the following equation may be correct only in isolated cases:

$$I = r/200 + 9 \quad (15)$$

In Figure 3 these equations are represented by Curve 1.

Equation $bB/100 = I + r + W + P$ may be rewritten as

$kB = I + r$ where $k = (b-w-p)/100$ and combining this with Equation 13 we get $B = (5r + 16)/4k$ (16)

and from Equation 14

$$B = (15r + r^2)/(r + 5)k \quad (17)$$

and from Equation 15

$B = (201r + 1800)/200k$, this may be changed to

$$B = (r + 9)/k \quad (18)$$

since 1/200 is a small quantity.

Equations 16, 17 and 18 are represented by the crosses on Curve 2, Figure 3.

In the application of this method to very small stores a modification should be adopted. It is apparent that the wage charge decreases very rapidly as the total sales decrease and a point is reached when a fixed percentage charge will not suffice for the payment of wages. Therefore, for so-called one man stores it is better to make a fixed charge instead of a percentage charge for both wages and net profit. The fundamental equation may then be written as

$$bB/100 - W - P = I + r.$$

By assuming the value 14 for W and P and substituting Equation 13 for I we obtain the equation

$$B = 100(5r/4 + 18)/b. \quad (19)$$

In the construction of the plot of Figure 3, b was given the value of 40 and k consequently became 0.15. By considering Equation 19 in conjunction with the crosses of Curve 2, it is noticeable that these points lie practically on a straight line. The equation of this line is

$$B = 6.75r + 45 \quad (20)$$

and it will be found that with the exception of low values of r this equation gives results which compare favorably with the equations previously mentioned.

In Table II computed values of B for given values of r, obtained by means of the above equations, are tabulated. Examination shows that Equation 20 suffices for all practical purposes.

TABLE II.

r.	I.			B.			
	13.	14.	15.	16.	17.	18.	19.	20.
0	4			26.7			45	45
4	5.0			60			57.5	72
6	5.5	5.4		76.7	76.4		63.8	85.4
8	6	6.2		93.3	93.3		70	97
10	6.5	6.7		110	111.1			112.5
20	9	8			186.7			180
50		9.1	9.3		393.9	393.3		382.5
100		9.5	9.5		730	726.7		720
120		9.6	9.6		864	860		855
150		9.7	9.8		1064.5	1060		1057.3
200			10		1398.3	1393.3		1395
400			11		2732.5	2726.6		2745

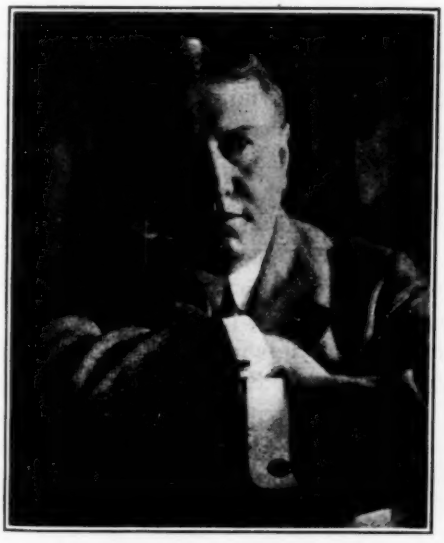
It may be advantageous to compare Equations 16, 19 and 20 for rentals between 0 and 4. This is shown in Table III.

TABLE III.

r.	16.	B. 19.	20.
0	26.7	45	45
1	35	48.1	51.8
2	43.3	51.3	58.5
3	51.7	54.4	65.3
4	60	57.5	72

When complete data are available the problem is very much simplified, but by means of this method the approximate total sales of a drugstore for a fixed rental can be readily computed.

LONG ISLAND CITY, N. Y.



O'Henry wrote part of his last story—"Let me feel your pulse"—in Asheville.

Ex-presidents John F. Hancock, of Baltimore, and Joseph L. Lemberger, of Lebanon, Pa.

GREATER SOCIAL RESPONSIBILITIES DEMAND A DEEPER INTEREST IN POLITICAL AFFAIRS.

Several years ago in an address, the lamented President Harding said:

"Team work finds its highest exemplification in the successful manufacturing organization. He who gives the most receives the most. The rewards of competitive industry do not go by favor but by capacity.

"We want in government the methods of industry, and we should avail ourselves to a greater degree than ever before of the wisdom of men who have made American industry one of the wonders of the modern world.

"The great technical professions form the cornerstone of material civilization. Their practitioners are derelict to their greater social responsibilities in their indifference to political affairs."

THE DEPARTMENT OF THE AMERICAN CONFERENCE OF PHARMACEUTICAL FACULTIES

[EDITOR'S NOTE.—At a time when we have in mind the expansion of the pharmaceutical curriculum any discussion of that subject will be welcomed. A committee of the Pharmacy Faculty of the University of Michigan has been working upon their own curriculum with the idea of making it at the same time more effective and more flexible. The result of that effort is contained in the article by Professor Charles H. Stocking, published in the present issue.

RUFUS A. LYMAN, *Chairman and Conference Editor.*]

THE REVISED CURRICULA OF THE UNIVERSITY OF MICHIGAN COLLEGE OF PHARMACY.

BY CHARLES H. STOCKING.

During more than fifty years of its existence, the College of Pharmacy of the University of Michigan has endeavored to serve all branches of the profession to the greatest possible advantage. Its graduates are to be found holding positions of trust and responsibility in widely divergent fields. Those who have gone out from the three-year, or Pharmaceutical Chemist course, have for the most part entered retail pharmacy. The four-year, or Bachelor of Science course, has contributed its alumni to analytical, manufacturing, teaching, journalistic and other important fields. Both of these courses have in the past been very rigid, offering little opportunity for elective studies. Thus, students who planned to take up one particular line of work after graduation were compelled by the inflexibility of the curriculum to elect practically the same studies as others who might be planning for a lifework of quite a different character. Realizing that this condition existed and believing that it would be advisable to liberalize the curricula for both degrees offered, the faculty began considering the matter more than a year ago.

As a result of frequent informal discussions over an interval of several months, the appointment of a special committee was authorized at a meeting of the faculty of the college in June, 1922. This committee was appointed by Acting Dean Edward H. Kraus at the opening of the current college year and was instructed to make a searching study of the problem. The committee consisted of two representatives from Pharmacy, two from the Department of Chemistry and one representative from the Medical School. The personnel of the committee was as follows: Chairman, C. C. Glover, Secretary of the College of Pharmacy and Associate Professor of Pharmacognosy; William J. McGill, Instructor in Pharmacy, Dr. Roy K. McAlpine, Assistant Professor of Analytical Chemistry; Dr. Chester S. Schoepfle, Assistant Professor of Organic Chemistry; and Dr. Herbert W. Emerson, Assistant Professor of Bacteriology and Head of the Pasteur Institute. The Committee presented a preliminary report in January of this year. This report was discussed in great detail and a number of recommendations were made by the faculty for consideration by the committee. At a subsequent faculty meeting held in March the final report of the committee was submitted. After a most careful consideration of the whole matter and following a very thorough study of the proposed revisions of the curricula, the faculty recommended them to the Board of Regents for adoption. On March 29, 1923, the Regents took formal action adopting the new curricula.

Under the new plan the three-year curriculum leading to the degree of Pharmaceutical Chemist is designed primarily for those students who wish to prepare for Retail or Commercial Pharmacy and differs but slightly in its general character from the old one. However, the number of hours required for graduation has been increased from 93 to 94, and includes the addition of a very desirable course in the History of Pharmacy.

The courses of study included in the three-year curriculum with the semester credit hours for these courses are as follows:

FIRST YEAR.

First Semester.		Second Semester.	
General Chemistry	4 hours	General Chemistry	4 hours
English	4 hours	Manufacturing Pharmacy	4 hours
Pharmaceutical Mathematics	4 hours	Hygiene	3 hours
Botany	4 hours	Commercial Pharmacy	2 hours
		Elective Subject	

SECOND YEAR.

First Semester.		Second Semester.	
Crystallographic and Optical Properties of Chemicals	2 hours	Organic Chemistry	4 hours
Qualitative Analysis	5 hours	Organic Chem. Laboratory	2 hours
Principles of Economics I	3 hours	Principles of Economics II	3 hours
Manufacturing Pharmacy	4 hours	Pharmacognosy	5 hours
Elective Subject		Alkaloids and Synthetics	2 hours

THIRD YEAR.

First Semester.		Second Semester.	
Prescription Pharmacy and Dispensing	3 hours	Prescription Pharmacy and Dispensing	3 hours
Pharmaceutical Chemistry	3 hours	Pharmacology	4 hours
Pharmacognosy	2 hours	U. S. P. and N. F. Drug Assaying and Pharmacopœial Testing	2 hours
Quantitative Analysis	5 hours	General Bacteriology	5 hours
History of Pharmacy	1 hour		

The plan of study for the four-year curriculum leading to the degree of Bachelor of Science in Pharmacy has been greatly changed. During the first two years all students will be required to take the same course of study, which includes the basic instruction. For the third and fourth years three distinct curricula are arranged, designed to prepare the students for either (A) General, Analytic, or Manufacturing Pharmacy; (B) for duties of Laboratory or Clinical Technician; or (C) for Pharmaceutical Administration. By this arrangement greater freedom in preparing for specific fields than heretofore is obviously possible. In general a larger number of electives is also permitted. However, in all cases the fundamental courses in Pharmacy, Chemistry, and allied sciences have been retained. The total number of hours required for graduation has been increased in all cases from 124 to 125 hours, and includes a required course in the History of Pharmacy. In the four-year curricula, leading to the degree of Bachelor of Science in Pharmacy, certain basic courses have been selected as required work for all students in the freshman and sophomore years. These courses are as follows:

FIRST YEAR.

First Semester.		Second Semester.	
General Chemistry	4 hours	General Chemistry	4 hours
Pharmaceutical Arithmetic	4 hours	Manufacturing Pharmacy	4 hours
English	4 hours	Mathematics	4 hours
German or French	4 hours	German or French	4 hours

SECOND YEAR.

First Semester.		Second Semester.	
Qualitative Chemistry	5 hours	Quantitative Chemistry	5 hours
Crystallographic and Optical Properties of Chemicals	2 hours	Hygiene	3 hours
Physics I	4 hours	Physics II	4 hours
Manufacturing Pharmacy	4 hours	Botany	4 hours

The Junior and Senior years permit of considerable diversification as to the choice of courses. Students who plan to become General, Analytical or Manufacturing Chemists will elect during their third and fourth years, the following required courses:

JUNIOR YEAR.

First Semester.		Second Semester.	
Organic Chemistry	5 hours	Organic Chemistry	5 hours
Prescription Pharmacy and Dispensing	3 hours	General Bacteriology	5 hours
Pharmacognosy Laboratory	4 hours	Pharmacognosy	5 hours
		Drug Assay and Pharmacopœial Testing	2 hours

SENIOR YEAR.

First Semester.		Second Semester.	
Food and Drug Analysis	3 hours	Pharmacology	4 hours
Bacteriology Laboratory	3 hours	U. S. P. and N. F.	4 hours
Pharmaceutical Chemistry	3 hours	Physical Chemistry	4 hours
History of Pharmacy	1 hour	Alkaloids and Synthetics	2 hours

In addition to these required courses, sufficient courses must be elected to complete a total of 125 hours. Suggested electives for the above curriculum are:

Food and Drug Chemistry	2–5 hours
Technical Microscopy	2–5 hours
Pharmacy Research	4 hours
Physical Chem. Laboratory	3–8 hours
Modern Physics	2 hours

For the student preparing for the duties of Laboratory or Clinical Technician, the following courses are required:

JUNIOR YEAR.

First Semester.		Second Semester.	
Organic Chemistry	5 hours	Organic Chemistry	5 hours
Prescription Pharmacy and Dispensing	3 hours	Physiological Chem. Laboratory	3 hours
Physical Chemistry	3 hours	General Bacteriology	5 hours
		Pharmacognosy	5 hours

SENIOR YEAR.

First Semester.		Second Semester.	
Bacteriology Laboratory	3 hours	Pharmacology	4 hours
Pharmaceutical Chemistry	3 hours	U. S. P. and N. F.	4 hours
Physiological Chemistry	3 hours	Laboratory Diagnosis	3 hours
History of Pharmacy	1 hour		

SUGGESTED ELECTIVE COURSES.

Water Analysis	3 hours
Histology	8 hours
Pathology	3–4 hours
Pathology tec. (summer session)	3 hours
Physical Chemistry	3–5 hours
Advanced Bacteriology	3 hours
Serum Reactions and Pathogenic Protozoa	3 hours

For the student preparing for pharmaceutical administration the following courses are required:

JUNIOR YEAR.

First Semester.		Second Semester.	
Organic Chemistry	5 hours	Organic Chemistry	5 hours
Prescription Pharmacy and Dispensing	3 hours	Prescription Pharmacy and Dispensing	3 hours
Principles of Economics I	3 hours	Principles of Economics II	3 hours
Accounting I	4 hours	Pharmacognosy	5 hours
History of Pharmacy	1 hour	Commercial Pharmacy	2 hours

SENIOR YEAR.

First Semester.		Second Semester.	
Bacteriology Laboratory	3 hours	General Bacteriology	5 hours
Pharmaceutical Chemistry	3 hours	Pharmacology	4 hours
Business Law I	3 hours	Physical Chemistry	4 hours
		U. S. P. and N. F.	4 hours

SUGGESTED ELECTIVE COURSES.

Business Law II	3 hours
Accounting II	4 hours
Money & Banking	3 hours
Corporations	3 hours

The course in Prescription Pharmacy and Dispensing has been extended over two semesters, instead of being given in one semester, and includes not less than 48 hours of service in the dispensing laboratories of the University Health Service and the University Hospital. Other equally important changes have been made.

The Faculty of the College believes that these revised courses of study will permit students to become better prepared for specific fields of endeavor than was possible under the old plan, without, however, making narrow specialists of them. The new plan is to become effective at the beginning of the college year, 1923–24, and will, it is believed, mark a distinct advance in pharmaceutical education.

Complete information concerning the new curricula is to be found in the announcement of the College of Pharmacy.

COUNCIL BUSINESS

A. PH. A. COUNCIL LETTER NO. 16.

(Abstract.)

WASHINGTON, D. C., July 27, 1923.

To the Members of the Council:

82. Program for Asheville meeting has been approved.

83. Election of active members. (Item 81.) Motion No. 29. Applicants Nos. 456 to 507 elected to active membership.

84. (Motion No. 30.) Motion to alter the program. It is moved by Dr. Arno Viehoever, seconded by A. G. DuMez, that provision be made for holding a joint session of the Scientific Section and the Section on Practical Pharmacy and Dispensing on Thursday evening, September 7, at 8:30 P.M. The following communication received from Dr. Viehoever July 21, 1923, explains the reason for this action.

"In accordance with your suggestion made during our recent conference on July 18, I am herewith returning my vote approving the tentative program of the forthcoming A. Ph. A. meeting, as it stands. I should like, however, to emphasize again, in writing, the wish that opportunity be presented us to hold a third session of the Scientific Section. As is no doubt well known, the Scientific Section, according to Section 6 of its By-Laws, published in the last Year Book, 1921, page xlvi, is to hold at least three sessions. Inasmuch as no meeting has been arranged for Thursday night, I would request that you secure approval of the Council for that time to be given over to the Scientific Section. It has been agreed by the respective sections to hold a joint meeting of the Section of Practical Pharmacy and Dispensing with the Scientific Section. Dr. Cook has consented to discuss the progress of the Pharmacopœia Revision, and Dr. Scoville that of the National Formulary.

"As mentioned in our circular letter, sent to many members of the A. Ph. A., we are making arrangements for a Stunt Show of useful apparatus, modifications of methods etc., to be given at one of our meetings. It is the plan to demonstrate these 'stunts' also on Thursday night, if possible, starting the meeting with a special popular lecture on Radio-activity. Professor Venable, formerly president of the North Carolina University, and past president of the American Chemical Society, now head of the Department of Chemistry, has promised to give us a talk on 'Radio-activity, Its Discovery, Nature, and Some of Its Revelations.'

"If these plans could be made possible we would be able to fill Thursday night with a very interesting meeting, with a record attendance."

85. Election of active members: No. 508, Casmer A. Sathre, 3332 Longfellow Ave. So., Minneapolis, Minn.; No. 509, Margaret M. Woods, 3132 43rd Ave. So., Minneapolis, Minn.; No. 510, Milton Dunn, Sheffield, Pa.; No. 511, Joseph Jacobs, 6 Marietta St., Atlanta, Ga.; No. 512, Thomas Alexander Cheatham, Room No. 122, State Capitol, Atlanta, Ga.; No. 513, Byron L. Rudh, Battle Lake, Minn.; No. 514, Adela Rosalind Aldes, 260 Aurora Ave., St. Paul, Minn.; No. 515, James William Coppedge, 117 E. Martin St., Raleigh, N. C.; No. 516, Thomas R. Adams, 432 East Railroad Ave., Wilmette, Ill.; No. 517, William J. Seward, Valley Junction, Iowa; No. 518, William John Husa, 324 E. Fairchild St., Iowa City, Iowa; No. 519, Geo. W. Swann, Madison, Minn.; No. 520, Wyly McG. Billing, Wm. S. Merrell Co., 5th & Pike Sts., Cincinnati, Ohio; No. 521, Kenneth Lester Bacon, 611 E. 18th Street, Minneapolis, Minn.; No. 522, Henry V. R. Moore, 187 Leslie St., Toronto, Ont., Canada; No. 523, Alfred L. Shellenberger, New Rockford, N. Dak.; No. 524, Reese Courts Harville, Main Street, Thomasville, N. C.; No. 525, Charles Borden Miller, Goldsboro, N. C.; No. 526, Polk Cleburne Gray, 100 Broad St., Statesville, N. C.; No. 527, Will E. Walker, The Anasarcin Chemical Co., Winchester, Tenn.; No. 528, Howard Edward Eichinger, Canby, Minn.; No. 529, Samson Christopher Malkewick, c/o Crookston Drug Co., Crookston, Minn.; No. 530, Victor O. Hanson, Arthur, N. Dak.

A. G. DUMEZ, *Secretary.*

A. PH. A. COUNCIL LETTER NO. 17.

(Abstract.)

WASHINGTON, D. C., Aug. 17, 1923

To the Members of the Council:

86. Applicants Nos. 508 to 530 elected to active membership.

87. Change in program of the annual meeting approved. It provides for holding a joint session of the Scientific Section and the Section on Practical Pharmacy and Dispensing on Thursday evening, September 7.

88. Election of active members: No. 531, Alexis Zephire Morin, Walhalla, N. Dak.; No. 532, George Kenneth Kraskin, 910—13th St., No., Fargo, N. Dak.; No. 533, David S. Simms, 716 West 2nd St., Hastings, Nebr.; No. 534, Axel E. Carlson, Danneborg, Nebr.; No. 535, Francis E. Cowger, Ainsworth, Nebr.; No. 536, Hazel Eleanor Landeen, Eagle Bend, Minn.; No. 537, Franklin Wills Hancock, Oxford, N. C.; No. 538, Erich Bruno Fritsch, 175—16th St., Milwaukee, Wis.; No. 539, Morris Snitzer, 4753a Newberry Terrace, St. Louis, Mo.; No. 540, Hodgdon Shaw, 26 Square, Bellous Falls, Vermont; No. 541, Louis J. Ehlert, 336 S. State St., Springfield, Ill.; No. 542, Jerome M. Peters, 519—12th St., Milwaukee, Wis.; No. 543, Cecil D. Lightfoot, 5737 W. Lake St., Chicago, Ill.; No. 544, Leonard N. Whitman, Cullman, Ala.; No. 545, Charles J. Tapscott, Joppa, Ala.; No. 546, Irving Kern, 134 Eldridge St., New York, N. Y.; No. 547, Howard Arthur Matthews, 349 E. 61st St., Chicago, Ill.; No. 548, Emil H. Dick, 1000 Washington St., Alten, Ill.; No. 549, Albert Martin Harrison, 1318 Walnut St., Murphysboro, Ill.; No. 550, Raphael Jacobson, 3156 Lawrence Ave., Chicago, Ill.; No. 551, James Thomas Underwood, Liberty, N. C.; No. 552, Joseph Drewry Joyner, Main Street, Franklinton, N. C.; No. 553, Jones Solomon Rudisill, N. Main St., Cliffside, N. C.; No. 554, Abraham J. Eisenberg, 1011 W. Harrison St., Chicago, Ill.; No. 555, John Algot Abrahamson, 5153 N. Clark St., Chicago, Ill.; No. 556, Clarence E. Barnhart, 1415 So. Adams St., Peoria, Ill.; No. 557, Cloyd S. Goodrum, Main St., Davidson, N. C.; No. 558, Norfleet Owen McDowell, Scotland Neck, N. C.; No. 559, George Walter Waters, Jr., 209 N. Virginia, Goldsboro, N. C.; No. 560, Jesse Powell Bradley, Burlington, N. C.; No. 561, Gordon Arnold Thaxton, Crystal Springs, Miss.; No. 562, Dan G. Waggoner, Cor. Main and Front St., Hattiesburg, Miss.; No. 563, Einar G. Eriksson, Cavalier, N. Dak.; No. 564, John Joseph Donahoe, Clare, Iowa; No. 565, Charles Stephan, Cor. Main and Center Streets, Marshalltown, Iowa; No. 566, Hubert Malcolm Parker, 601 S. Dearborn St., Mobile, Ala.; No. 567, George W. Koenig, 19 Central Ave., S. W., LeMars, Iowa; No. 568, Wilber Eugene Corbin, Lander, Wyoming; No. 569, Omer C. Boshart, Wayland, Iowa; No. 570, Gaile Osro Putnam, 101 E. Miner Ave., Ladysmith, Wis.; No. 571, Gerald Silvester Scivert, Grafton, N. Dak.; No. 572, Arthur W. Quan, 301 So. Mills St., Madison, Wis.; No. 573, Lee Goldsmith, 1838 Diamond St., Philadelphia, Pa.; No. 574, Amos Leopold Hamaker, 20–22 W. King St., Lancaster, Pa.; No. 575, Caroline S. Peiffer, 2901 E. Thompson St., Philadelphia, Pa.; No. 576, Francis Patrick Kelly, Main St. and 7th Ave., Carbondale, Pa.; No. 577, Frederick Harry Woods, 130 Prospect, Sharpsville, Pa.; No. 578, Samuel Urffer, 2860 N. 5th Street, Philadelphia, Pa.; No. 579, Charles Morgaret States, Dodge City, Kansas; No. 580, Carl O. Selig, 514 State St., Augusta, Kansas; No. 581, Charles N. Murray, 21st and Strong, R. R. No. 7, Topeka, Kans.; No. 582, C. C. Strahan, c/o Union News Drug Co., Parsons, Kans.; No. 583, J. E. Wiggs, 1009 Park Ave., Kansas City, Kans.; No. 584, William A. Billingslen, 3117 Prospect, Kansas City, Mo.; No. 585, Orin F. Clopp, Arlington, Kans.; No. 586, William Darius Kelley, Main St., North Troy, Vermont; No. 587, William M. Stauffer, 147 E. Main St., New Holland, Pa.; No. 588, W. F. Welborn, Lexington, N. C.; No. 589, Geo. Ernest Burwell, Cor. 9th and Caldwell Sts., Charlotte, N. C.; No. 590, Ernest L. Hicks, Union St., Concord, N. C.; No. 591, Wallace Alfred Tompkins, Jackson, Ala.; No. 592, Charles S. Haupt, 502 Cavitt Ave., Trafford, Pa.; No. 593, Frederick George Luebert, 1418 N. Fourth St., Philadelphia, Pa.; No. 594, Ralph L. Welsh, 1616½ Union Ave., Altoona, Pa.; No. 595, Howard G. Isby, 312 South State St., Clark's Summit, Pa.; No. 596, Luther M. Nemon, 33 Connellsville St., Dunbar, Pa.; No. 597, John Robert Hughes, Madison, N. C.; No. 598, Edward L. Tarkenton, West Nash St., Wilson, N. C.; No. 599, Ben Lee Young, Huntsville, Ala.; No. 600, N. J. Bleser, Milbank, S. Dak.; No. 601, Vesta C. Abar, 3045—3rd Ave., So., Minneapolis, Minn.; No. 602, Arthur R. Wiele, 609 Oak Lane, Albert Lea, Minn.; No. 603, Joseph M. Armitage, Princeton, Minn.; No. 604, Frederick Colbert, No. 1 South Main St., Butte, Mont.; No. 605, G. Claude Drake, 317 So. State St., Ann Arbor, Mich.; No. 606, Wellington Travis, 2633 Woodward Ave., Detroit, Mich.; No. 607, Walter John Wilson, 1718–20 David Whitney Bldg., Detroit, Mich.; No. 608, John B. Bardonski, 1256 Noble St., Chicago, Ill.; No. 609, William Elmer Mercer, Liberty, Ill.; No. 610, John Cogdell Hood, 203 N. Queen St., Kinston, N. C.; No. 611, Ole J. Lee, Pelican Rapids, Minn.; No. 612, Chauncey Calvin Bower, 665 Central Park Pl., St. Paul, Minn.; No. 613, John Joseph Lane, 280 Suydam St., Brunswick, N. J.; No. 614, Benjamin

Franklin Moseley, Wilson Ave., Thomasville, Ala.; No. 615, Walter Norville Bagby, N. W. Cor. Central and Halley, Armstrong, Mo.; No. 616, G. Ernest Newman, Canton, Pa.; No. 617, William L. Bucher, 403 Locust St., Columbia, Pa.; No. 618, Sister Mary Paul, Charity Hospital, Central and E. 22nd St., Cleveland, Ohio; No. 619, Harry Erskine Fiers, 2510 Park Blvd., Detroit, Mich.; No. 620, Mrs. Pauline Kurz, 2520 Michigan Ave., Detroit, Mich.; No. 621, Howard G. Haines, Sandusky, Mich.; No. 622, C. Wilbur Parker, Horner, Mich.; No. 623, Andrew Palmerston Young, 1977 Grand River Ave. W., Detroit, Mich.; No. 624, Dallas Dow Alton, No. 1 Main St., W., Fremont, Mich.; No. 625, Charles H. Abbott, West Branch, Mich.; No. 626, John Gabric, 201 W. 22nd St., Chicago, Ill.; No. 627, A. B. McConnell, 1824 Farnum St., Omaha, Nebr.; No. 628, J. F. Schulte, Van Hook, N. D.; No. 629, Roy Bird Cook, 1559 Lee Street, Charleston, W. Va.; No. 630, Wiley E. Miller, 627 10th Ave., S. E., Minneapolis, Minn.; No. 631, G. Turner Haines, 423 So. 16th St., Omaha, Nebr.; No. 632, Volney K. Young, Main Street, Waterbury, Vermont; No. 633, W. W. Pratt, 1 Elm, Manchester Depot, Vermont; No. 634, William Bond Gould, Glenwood, Arkansas; No. 635, Finley Reid Beason, 514 Line St., Decatur, Ala.; No. 636, Beatrice Averitt, Fayetteville, N. C.; No. 637, Reginald D. Black, Gilman City, Mo.; No. 638, Adolph W. Scharping, Arlington, Minn.; No. 639, Cornelius N. McGillwray, 318 Main St., Valley City, N. Dak.; No. 640, Severin Almkolv, Cooperstown, N. Dak.; No. 641, Henry Edgar Close, Langdon, N. Dak.; No. 642, Harry L. Cox, 21 W. Main St., Ephrata, Pa.; No. 643, Edward J. Rihm, 5th Ave. and 10th St., Ford City, Pa.; No. 644, Susie Nielsen Schram, 11 N. Gold St., Lead, S. Dak.; No. 645, John Momsen, Alexandria, S. Dak.; No. 646, Otto W. Wickham, Seaside Park, N. J.; No. 647, Jarner Edward Hand, 45 Kearny Avenue, Kearny, N. J.; No. 648, John H. Coleman, 398 Summer Ave., Newark, N. J.; No. 649, E. T. Beddingfield, Clayton, N. C.; No. 650, Marion Arthur Carrington, Onarga, Ill.; No. 651, Harry Francis Reinert, Colfax, Wis.; No. 652, Jeston A. Mathews, Hedrick, Iowa; No. 653, Clyde Eubanks, Chapel Hill, N. C.; No. 654, Chas. M. Fox, Asheboro, N. C.; No. 655, Germain Bernard, 106 Corcoran St., Durham, N. C.; No. 656, James Callahan, Vick Chemical Co., Greensboro, N. C.; No. 657, Joseph Paul Gamble, Monroe, N. C.; No. 658, C. E. Matthews, Roanoke Ave., Roanoke Rapids, N. C.; No. 659, Hiram Grantham, Red Springs, N. C.; No. 660, Edwin Nowell, 113 S. Elm St., Greensboro, N. C.

A. G. DuMez, *Secretary.*

NATIONAL ASSOCIATION OF RETAIL DRUGGISTS IN BOSTON.

The "Silver Anniversary Meeting" of the National Associaton of Retail Druggists will be held in Boston during the week of September 24. The local committees have made preparations for a large convention. A rate of a fare and one-half has been secured for the round trip; identification certificates should be secured at once from the N. A. R. D. Office in Chicago; they are available for all members, whether delegates or not. Arrangements should be made for hotel accommodations early.

One of the subjects for discussion during the meeting will be "Price Maintenance," and an entire evening has been set aside for a discussion of this very important question. Among the speakers will be Hon. Clyde Kelly and Attorney Charles Wesley Dunn; the former is the author of the Kelly price maintenance bill and the latter prepared the briefs in the Colgate and Beech-Nut Cases. Association attendance is a duty, has a value for the member and encourages the officers.

MILWAUKEE MEETING OF THE AMERICAN CHEMICAL SOCIETY.

The American Chemical Society will meet in Milwaukee, Wis., during the week of September 10.

A rate of one and one-half fare under the *certificate plan* has been granted by most railroads to those attending the Milwaukee meeting of the American Chemical Society, provided there is an attendance of at least 250 who will bring with them regularly issued certificates obtained from ticket agents at starting points and present them for validation at the convention registration desk.

A part of the program of the Section on Chemical Education of the American Chemical Society, for the Milwaukee meeting, consists of a joint symposium with the Division of Industrial and Engineering Chemistry and the Chamber of Commerce of the City of Milwaukee. The subject to be discussed is "Industrial Chemical Education and the Importance of Coöperation between Educational Institutions and the Industries."

EDITORIAL NOTES

Editor: E. G. EBERLE, Bourse Building, Philadelphia, Pa.

Committee on Publication: A. G. DUMEZ, *Chairman;* S. L. HILTON, H. M. WHELPLEY, R. A. LYMAN, W. L. SCOVILLE, and the Editor-in-Chief of the JOURNAL, General Secretary, Treasurer and Reporter on the Progress of Pharmacy, *ex-officio*.

Collaborators: JULIUS A. KOCH, President, A. Ph. A.; CHARLES H. LAWALL, President, A. C. P. F.; EDWARD WALSDORF, President, N. A. B. P.; E. FULLERTON COOK, Chairman, U. S. P. Revision Committee; W. L. SCOVILLE, Chairman N. F. Revision Committee; S. L. HILTON, Chairman, Council A. Ph. A. The Chairmen of the Sections, A. Ph. A.: ARNO VIEHOEVER, CROSBY B. WASHBURNE, W. F. GIDLEY, WALTER M. CHASE, CLYDE L. EDDY; E. F. KELLY and WILLIAM B. DAY of the House of Delegates; A. G. DUMEZ, Secretary of the Council, the General Secretary, and the Reporter on the Progress of Pharmacy.

INSULIN.

In his address as Chairman of the British Pharmaceutical Conference Mr. F. W. Gamble gave an interesting review of some of the more recent organotherapic preparations called for in present-day pharmacy. From this portion of the address we quote his remarks on insulin, in part:

"The story of insulin should possess a special interest for pharmacists. Physiological experiments had shown that the existence of such a hormone in the pancreas was certain; the name Insulin was given to it by Schafer many years before a means of separation was found. Different lines of research had converged upon the islets of Langerhans, so named after their discoverer, distributed through the lobules of the pancreas as the seat of elaboration of insulin. The islet tissue is in intimate relation with the blood vessels of the pancreas, but is remote from the acinous cells which secrete the pancreatic zymogens. Many attempts to prepare an extract of pancreas containing the antidiabetic principle had failed, in spite of unequivocal evidence of the presence of such a principle in the pancreas during life. The idea presented itself to Dr. Banting, of Toronto, that the principle might be lost in the process of extraction, not because of its own instability, but possibly through the destructive agency of the powerful ferments secreted by the pancreas. It was well known that by tying the pancreatic duct a partial degeneration of the pancreas could be brought about. This degeneration affects the cells secreting the digestive ferments, leaving the islet tissue and its blood capillaries intact. Such a partially degenerated pancreas might yield an active preparation of the islet principle, and experiment showed this to be the case. The activity of such a preparation was destroyed by boiling or by contact with pancreatic juice. Means were now devised for extracting normal pancreas by means of a solution that inhibited the tryptic ferment; an extract made with acidulated alcohol was found to be active and capable of keeping alive a depancreated dog. Experiments were then instituted to obtain a preparation from ox pancreas suitable for use in human diabetes. It was found that 50 per cent. alcohol extracted insulin from finely minced pancreas, whilst inhibiting the tryptic ferment. If the alcoholic strength of this solution be raised to 80 per cent., insulin is retained in solution whilst other substances are precipitated. This alcoholic solution is concentrated *in vacuo* at a very low temperature; fats and lipoid substances are removed, and crude insulin is precipitated from the concentrate with absolute alcohol. The crude insulin is further purified by re-solution, precipitation as picrate, and conversion into the readily soluble hydrochloride. The process requires the most absolute control if loss of activity is to be avoided. Insulin is destroyed by heat, except for short periods in strongly acid solutions. Alkaline solutions lose their activity even at body temperature. It is readily absorbed by filtering media if its solutions have a hydrogen-ion concentration near the isoelectric point. The activity of insulin requires to be determined by physiological experiment. The dose is expressed in arbitrary units which represent the amount of insulin required to produce a certain effect when injected into a rabbit; the usual dose is 10 units. Insulin is destroyed by the digestive ferments, and cannot therefore be administered orally. Subcutaneous injections are given twice daily. Insulin treatment enables the

diabetic patient to assimilate carbohydrate; the immediate result of an injection is to cause a fall in the percentage of sugar present in the blood."

THE INTERNATIONAL PHARMACEUTICAL FEDERATION AND LEGISLATION AFFECTING PHARMACY.

The International Pharmaceutical Federation at its recent convention in London approved resolutions presented by delegate C. L. Butchers, which provide that when in the future new legislation is proposed affecting pharmacy, the various governments should be asked to confer and coöperate with the respective National Pharmaceutical Associations. The Federation expressed the opinion that adequate representation should be accorded to pharmacists on all committees controlling state health dispensing. Another resolution presented by Mr. Butchers asked that the Federation affirm the principle that an adequate dispensing fee be charged by pharmacists in all cases where professional services are rendered. The first resolution was approved and the latter was referred for further consideration.

INTERNATIONAL STANDARDIZATION OF CINCHONA BARK AND ITS PREPARATIONS.

In a paper presented before the British Pharmaceutical Conference, C. T. Bennett recommends that cinchona bark and its preparations be standardized by international agreement. He considers that the importance of the drug merits such consideration. The paper presented is comprehensive and shows that not only do the galenical preparations vary according to the proportion of alkaloids and extractive in the bark but the preparations official in the pharmacopœias of different countries differ in formulas and in alkaloidal strength.

Mr. Bennett recommends that the bark should be standardized for total alkaloids by titration and the limits fixed for galenical preparations should be based on barks with from 6 to 8 per cent. of total alkaloids.

THE ACTIVITY OF PHARMACOPŒIAL PREPARATIONS OF ERGOT.

A. J. Clark and W. A. Broom reported on the activity of pharmacopœial preparations of ergot before the Scientific Section of the British Pharmaceutical Conference; comparisons of the fluidextracts of the British and U. S. Pharmacopœias. Various physiological assay methods are given in the paper. In the introduction of the subject the authors state that "unfortunately, ergot contains a large number of pharmacologically active substances, and there is no general agreement as to which of these is the most important. Clinical evidence gives little help in this matter, for clinicians appear to be equally satisfied with the most varied assortment of ergot preparations, and many of the preparations in clinical use appear from pharmacological tests to be almost completely inert. The active constituents of ergot consist of the specific alkaloids ergotoxine and ergotamine, and a group of amines, which latter bodies can be obtained from many other sources."

The action of ergot and the different methods of assay are explained in the paper; the processes for various preparations, chiefly of the British Pharmacopœia, are outlined; in part to explain the findings. The conclusions arrived at by the authors, which were sustained by those participating in the discussion, follow:

(1) The methods of standardizing ergot preparations upon the isolated uterus or upon the cat's uterus *in situ* measure chiefly the amine content of the ergot preparation.

(2) The action of ergot preparations in reversing the action of adrenalin upon the isolated rabbit's uterus can be made the basis of a convenient method of standardizing ergot preparations. The method measures only the content in ergot alkaloids and very small quantities of these can be detected. The results obtained agree with the results obtained by the cock's comb method and the cat's blood pressure method.

(3) The instructions of the British Pharmacopœia, if followed exactly, result in preparations almost completely devoid of ergot alkaloids, although from the same samples of ergot the U. S. P. method extracts considerable quantities of ergot alkaloids. The B. P. method can, however, be modified so that a certain proportion of the ergot alkaloids are obtained.

(4) Since the ergot alkaloids are the only known active principles of ergot that are specific to ergot the methods of preparation laid down in the B. P. appear to be frankly absurd.

U. S. PUBLIC HEALTH SERVICE INFORMS VACATIONISTS RELATIVE TO POISON IVY.

The Naval Radio Station, Arlington, and broadcasting stations have been releasing health hints for vacationists; recently in-

formation has been given out relative to poison ivy. There are many plants that have more or less similar toxic properties, among them: Aconite, ailanthus, asparagus, catalpa, dog fennel, lady's slipper, wild carrot, hop, lobelia, oleander, nightshade, ox-eye daisy, parsnip, pokeweed, smartweed, primula, buttercup, poison elder or poison dogwood, bloodroot, mullein, cocklebur, and the mustards.

Gasoline is said to be effective against poisonings from these sources, especially when applied soon after contact. Sodium chloride, sodium bicarbonate, boric acid are among the well-known household remedies.

WHO PAYS FOR ADVERTISING?

The Associated Advertising Clubs of the World have stated that a billion dollars was expended for advertising in the United States during the year 1922.

Some persons claim that advertising increases the cost of commodities to consumers; others emphatically deny this statement.

The production cost of any commodity depends largely upon the volume of goods produced, and the advertiser claims that by the use of advertising he increases his output so that his costs are substantially less and this enables him to make a much lower price on his commodity to the consuming public.

Without advertising manufacturing would become a small scale proposition and the economies effected by volume production would be lost to the public. Advertising also educates the public to a better understanding of commodity values and it materially increases the volume of sales by dealers.

Price cutting of standard, branded articles undermines the efficiency of advertising, because it casts suspicion upon the advertised goods. If one retailer sells a 50c article for 34c the public reasons that the dealer who charges the standard price is profiteering. This is a demoralizing influence. It undermines the value of advertising and reacts to the detriment of the manufacturer as well as the dealers.

Standard goods at standard prices increase the efficiency of advertising and this, ultimately, means lower prices to the consumer.—*The Pharmaceutical Era.*

A COLLECTION IDEA.

A check was received by an Atlanta store recently drawn on a local bank in the sum of $5, but which the sender had forgotten to sign. It came in a printed return envelope, but not being accompanied by a letter or note of any kind the company had no way in the world of ascertaining who had sent it.

The idea occurred to William F. Greene, manager of the department, to send out several letters to old Atlanta accounts, telling of this check and asking the one who had sent it to let the company know, so it could be returned for signature and duly credited to his account. It was not Greene's idea merely to find out who had sent the $5 check, but he thought such a letter would have a good moral effect on those receiving it and result in several making payments on their accounts.

The letter used was multigraphed and filled in individually with the customer's name and address—an important point in making use of this idea. Seventy letters were sent out to a selected list of rather old accounts, the copy reading as follows:

"Through the mail this morning we received check, No. 1556, drawn on the Atlanta National Bank and payable to our order, for $5.

"This check was not signed, and, being unaccompanied by a letter or note of any kind, we are unable to ascertain the identity of the sender.

"Thinking that you may have sent this check we thought it best to write you this letter regarding it.

"Please let us know if this check should be credited to your account, and we will return it at once for your signature.

THE GEORGE MUSE CO."

Out of seventy letters sent, forty replies were received in one week, and in these forty replies there were twenty-three checks. There was one check for $56.50 for payment in full, another for $50 for part payment on an account, a third and fourth for $31 and $30, respectively, and a fifth and sixth for $25 and for $22.13, respectively. Of the others the amounts were from $15 down to $5, and there were several checks for the latter sum.

Furthermore, all the customers replying to the letter, with possibly two or three exceptions, promised payment shortly if they were not among the twenty-three who sent checks, while two telephoned the store and one called personally.

It is the company's intention, says the *Motor World*, to use this plan regularly hereafter on old standing accounts.

Incidentally the sender of the unsigned

check is still unknown.—Through *Bulletin of Pharmacy*.

THE THOMPSON INSTITUTE FOR PLANT RESEARCH.

A statement issued recently by Dr. William Crocker, Research Director of the new Thompson Institute for Plant Research which Colonel William B. Thompson is establishing in Yonkers at a first cost of more than $500,000, gave details of the plan by which powerful electric lamps are to supplement sunlight in growing plants. "This new institution with its gardens, greenhouses and laboratories," said Mr. Crocker, "is to be to plants and flowers what the Rockefeller Institute is to humanity. In other words, it is to study and try to cure diseases of plants and flowers and other vegetation. Eventually the institution is to cost $2,500,000. Seeds from the tomb of King Tutankhamen will be tested for germination in the new laboratory.—From *Scientific American*.

CENTENARY OF JEAN HENRI FABRE.

The French entomologist, Jean Henri Fabre, was born at St. Léons, December 21, 1823. On the 6th of last month a series of fêtes was begun at Millau to honor the man whose interesting studies of insect life became known only a few years before his death. Since then his books have been translated into the principal languages. The principal ceremony was the unveiling of a statue of the scientist by the sculptor Malet.

PERSONAL AND NEWS ITEMS.

Dean Wortley F. Rudd of Richmond, Va., and **W. L. Cliffe** of Philadelphia were registered at the recent meetings in London of the International Pharmaceutical Federation and British Pharmaceutical Society.

Dr. A. R. Bliss has accepted the professorship of Pharmacology and Physiology in the College of Medicine and Dentistry and the School of Pharmacy, University of Tennessee.

James E. Bartlett, former president of Parke, Davis & Co., and identified with that company in various capacities from 1889 to 1921, has purchased a controlling interest in the Pitman-Moore Company, pharmaceutical and biological chemists, Indianapolis, of which corporation he is the president and general manager.

E. G. Swift, secretary and comptroller of Parke, Davis & Co., has retired from active business life after forty years' connection with the company he has served in various important capacities.

Hugh O'Connor, well known to druggists of California through his former connection with the office of the narcotic division of the internal revenue department in San Francisco, has joined the staff of the *Pacific Drug Review* as its field representative.

Mr. and Mrs. R. D. Keim and **F. W. Nitardy** have returned from an extended tour and vacation trip to the Pacific coast and Canadian resorts.

Prof. H. A. Langenhan contributed an interesting historical article on "Digitalis" to the August *Pacific Drug Review;* a list of preparations of digitalis is given and the synonymy of digitalis and its preparations of the United States Pharmacopœia from 1820–1920.

Thomas J. Keenan, formerly editor of *Paper*, is now editor of the publications of Lehn & Fink, and located at their laboratories in Bloomfield, N. J.

William H. Schuller, president of the Oregon Drug Clerks' Association, has been appointed member of the Oregon State Board of Pharmacy by Governor Pierce.

W. Bruce Philip has graduated in law. He also holds the chair of "commercial pharmacy" in the University of California. In conjunction with other duties Mr. Philip found time to continue his law studies and earned the degree of LL.B.

John McKesson, New York, and **James W. Morrisson** are in Europe, seeking rest and pleasure.

J. T. Coulson, an ex-president of Texas Pharmaceutical Association, is now president of Texas Drug Company of Dallas. The wholesale drug corporation has recently been reorganized—it was established in 1894 and is one of the larger wholesale drug houses of the southwest.

M. Schlesinger and **Dr. Wm. C. Anderson** related early experiences at a recent meeting of New York Veteran Druggists' Association. The former gave an interesting account of his start with the late Samuel J. Bendiner. The latter was a graduate of the University of Vienna. He was active in the compilation of the "New York and Brooklyn Formulary," and one of the five who constituted the editing committee; at the Pittsburgh A. Ph. A. meeting, the Formulary was offered to and accepted by the Association, the offer being made by Mr. Bendiner for the committee.

Mr. Schlesinger names his preceptor "the father of the National Formulary." Mr. Bendiner joined the American Pharmaceutical Association in 1882; he died February 20, 1897.

Emil Roller presented a paper on M. Louis Pasteur at a recent meeting of the German Apothecaries' Society.

Dr. Henry Kraemer was an honor guest of Utah Pharmaceutical Association; the subject of his address was "The Masters of Pharmacy."

OBITUARY.

N. EMERY WILLIAMS.

N. Emery Williams, well and favorably known pharmacist of St. Louis, died at his home, after a lingering illness, aged 50 years. Mr. Williams was proprietor of the drug store in the Metropolitan building, Grand Boulevard and Olive Street, where he had built up a flourishing business which was limited to the filling of prescriptions.

The deceased was born at Rushville, Illinois, and educated at the Northwestern University, Evanston, Illinois. He is survived by his widow. Mr. Williams joined the American Pharmaceutical Association in 1912.

MISS ANNIE M. PATTERSON.

Miss Annie M. Patterson died August 4, at the home of her mother in Baltimore, after an illness of a year or more. Miss Patterson attended high school in Baltimore and then the University of Maryland. She graduated from the Department of Pharmacy, U. of M., ranking second in her class. She was for a time employed with Messrs. Hynson, Westcott & Dunning and later with Morgan & Millard. For a time the deceased resided in Denver where she was connected with the Chemical Manufacturing Company.

Miss Patterson joined the American Pharmaceutical Association in 1915, was a loyal alumna, a member of Maryland Pharmaceutical Association, deeply interested in pharmacy and beloved by all who knew her.

CARL G. KREMERS.

Sympathy is expressed to Dr. and Mrs. Edward Kremers in their bereavement by the death of their son, Carl G. Kremers, of scarlet fever. The young man was a junior in the College of Letters and Science at the University of Wisconsin and was registered in the course in chemistry.

SUBSCRIPTIONS TO AMERICAN PHARMACEUTICAL ASSOCIATION HEADQUARTERS BUILDING FUND.*

No.		
	Previously reported	$7,506.90
168.	Chas. G. Westbrook, Newbern, Tenn. (Paid)	5.00
169.	Charles P. Greyer, Morgantown, N. C. (Paid)	12.50
170.	Fred W. Rauth, Springfield, Ill.	25.00
171.	John Stuchlik, Chicago, Ill.	10.00
172.	Carl C. Rennecker, Wilmette, Ill. (Paid $10.00)	50.00
173.	Fred L. Pfaff, Centralia, Ill.	25.00
174.	Paul Eiche, Effingham, Ill. (Paid $5.00)	25.00
175.	W. F. Baeslau, Chicago, Ill.	25.00
176.	Edward Stuchlik, Berwyn, Ill.	50.00
177.	Albert Zimmerman, Peoria, Ill. (Paid $10.00)	50.00
178.	George Zoeller, Chicago, Ill. (Paid $10.00)	50.00
179.	Wm. D. Duncan, Ottawa, Ill. (Paid $100.00)	500.00
180.	James P. Crowley, Chicago, Ill.	25.00
181.	J. B. Michels, El Paso, Ill. (Paid $5.00)	25.00
182.	Illinois State Pharmaceutical Association (Paid $100.00)	500.00
183.	Herman Fry, Chicago, Ill. (Paid $10.00)	50.00
184.	H. Mayber, Chicago, Ill. (Paid $5.00)	25.00
185.	John A. Mertes, Chicago Ill. (Paid $5.00)	25.00
186.	Harold N. Bruun, Chicago, Ill. (Paid $5.00)	25.00
	Total	$9,009.40

* For preceding reports on funds see Volume XI, 1922, JOUR. A. PH. A., pp. 392, 644, 872; Volume XII, pp. 90, 555.

SOCIETIES AND COLLEGES.

THE FOURTH GENERAL ASSEMBLY OF THE INTERNATIONAL PHARMACEUTICAL FEDERATION.

The International Pharmaceutical Federation held its annual meeting in London, July 23. Editorial comment has been made relative to the transactions reported. Professor van Itallie, Dean of the University of Leyden and President of the Federation, was in the chair, supported by Mr. E. T. Neathercoat, Dr. J. J. Hofman (Secretary), and Dr. A. Schamelhout (Belgium). Among other delegates and members of the Conference present were: Sir Wm. Glyn-Jones, Messrs. Edmund White, J. Loisel (France), Cav. F. Pratta (Italy), J. Cofman-Nicoresti (Roumania), Dr. Angel Morales (Spain), C. Rousseau (France), Prof. E. Emanuel (Greece), E. Collard, A. Bouville (France), C. L. Butchers (Australia), A. J. Jones, C. T. Bennett, Prof. Greenish, E. Saville Peck, H. B. Stevens, H. Lucas, J. P. Ellerington, W. A. Jones (Liverpool), R. Marloum (Egypt), H. Finnemore, and Misses Elsie Hooper, S. M. Snellus, and Marie Shaw.

LIST OF DELEGATES.

Bennett, R. R., London
Bouville, A., Association Générale des Syndicats Pharmaceutiques de France
Butchers, C. L., Secretary, Pharmaceutical Society of Victoria
Butchers, Mrs., Victoria
Chambers, Miss, Victoria
Cliffe, W. L., American Pharmaceutical Association, Philadelphia
Cofman, Jules, London
Cofman, Victor, London
Collard, E., Association Générale des Syndicate Pharmaceutiques de France
Daminet, F., La Nationale Pharm., Bruxelles
Daminet, Mlle., Bruxelles
Dries, A. F. M. van den, Nederlandsche Maatschappij ter Bevordering der Pharmacie
Emmannuel, Prof. Dr. E., Société Panhelleniques des Pharmaciens
Gamble, F. W., London
Greenish, Prof. Dr. H. G., London
Glyn-Jones, Sir W. S., London
Grimbert, Prof. Dr., Association Générale des Syndicats Pharmaceutiques de France
Hofman, Dr. J. J., Secretary General, La Haye
Itallie, Dr. L. van, President, Leyden
Itallie, V. van, Nederlandsche Maatschappij ter Bevordering der Pharmacie
Janzon, Hilding, —
Lacroix, —, du Syndicat Général des Pharm. de France, Paris
Langrand, A., Paris
Langrand, Marg. Mlle., Paris
Loisel, J., Vice-President, Beauvais
Masloum, Renalto V., Cairo
Morales de las Pozas, Dr. Angels, Union Pharmaceutica Nacional, Madrid
Neathercoat, E. T., Weybridge
Pattou, B., La Nationale Pharm. Bruxelles
Peck, E. Saville, Cambridge
Pratta, Cav. Francesco, Secretary General, Pharmaceutical Societies of Italy
Rousseau, Célestin, Levallois Perret, Sec. "Internacia Scienca Ascio"
Rudd, Dr. W. F., American Pharmaceutical Association, Richmond, Va.
Sargeant, F. Pilkinton, Leeds
Schamelhout, Dr. A., Secretary, Bruxelles
Schamelhout, Mme., Bruxelles
Vocadlo, Dr. M. P., Czecho-Slovakia
White, E., London

THE NATIONAL WHOLESALE DRUGGISTS' ASSOCIATION MEETING IN CLEVELAND.

The Committee on Rates and Routes of the National Wholesale Druggists' Association in a recent bulletin announces that transportation arrangements have been made for members and families who will attend the Forty-ninth Annual Meeting to be held at the Hotel Cleveland, Cleveland, Ohio, October 8–12, 1923.

The Passenger Associations have granted a rate, a fare and one-half of the current one way fare on the convention certificate plan contingent upon an attendance of 250 or more members and delegates. Members are strongly urged in purchasing tickets to Cleveland who do not expect to return at once or by the same route, to ask for a convention certificate. Unless this is done the committee will not be able to secure the half fare for members on return trip.

CHEMICAL STUDY COURSE A FEATURE OF THE NINTH NATIONAL EXPOSITION OF CHEMICAL INDUSTRIES.

The Ninth National Exposition of Chemical Industries will be held at Grand Central Palace, New York City, September 17 to 22. An added feature of the Exposition is the course offered in the fundamentals of chemical engineering and industrial practice. The course will be under the direction of Prof. W. T.

Read, of Yale University, a member of the Exposition Advisory Committee. The topics to be dealt with will include plant equipment, materials of construction, and the distribution of chemicals in commerce. The speakers will include well-known chemical engineers, among them Galen H. Clevenger; W. H. McAdams, of M. I. T.; A. E. Marshall, Baltimore; Harry Carlson; S. G. Ketterer; G. L. Montgomery; W. S. Calcott, du Pont; Ross C. Purdy; O. I. Charmann; and Homer Hendricks.

There will be no charge made to the students attending this course, and already through their instructors, through whom registration cards may be secured, over 150 students have applied for admission. In view of the wide interest, Columbia University has offered the use of its dormitories to those attending during the week of the exposition, making a charge of $1.50 per night for rooms.

THE PHARMACIST AND THE LAW.

THE BRAND'S THE THING.

Liberty is taken in reprinting the following editorial under above caption which appeared in the *New York Commercial* of July 23:

"More and more the brand is becoming a solid factor in business. Francis A. Adams is rendering a real service to American industry by emphasizing the importance of the brand as an asset in continuous advertising.

"Ancient is the story, the honor and the service of the brand. It had become a notable element in trade advertising long before the Asiatic or European discovery of any sort of printing process. It was a factor in the seeking, gaining and holding of trade many centuries before Ibn. Batutu or Marco Polo wrote their first overseas and overland trade reports. How old the brand actually is would be difficult even to guess.

"That it was a multicentenarian long before David or Solomon was born is an established fact of history. After the collapse of the Roman empire, while Europe was giving birth to modern western civilization, trade in that part of the world fell into the hands of the sharper and 'long-shotter.' The chief industries and finer crafts were appendages of the feudal barons. Both the iron trade and the linen trade were born in the castle—the iron trade at the forge of the armorer, the linen trade (and, therefore, the cotton trade) at the spinning wheel of the chatelaine and her bodywomen. By his own skill and his own will the armorer won his economic freedom. His 'mark' or brand on sword or spear or helm was the advertisement that brought him trade. One can readily imagine what wonderful publicity stunts might have been pulled in those brave old days if only the knight and the armorer could have been blessed with newspapers. How Mark Twain would have relished the chance of doing justice to the stout blade that enabled Sir Hagen of Trony to skiver and skewer Gunther's enemies? Yet, from what we can learn (taking their cue from the motto of Abraham Lincoln), those armorers of old 'did the best they could with the instruments at hand.' So, too, did the guilds. They gave us the hall-mark, parent of the trade-mark, and they paved the way for the patent laws and the brands of today. Quality had become a valuable consideration, a protection against the unscrupulous trader.

"Now the brand possesses a relative value undreamed of by the traders of Tyre, of Damascus, of Novgorod, of Kiao-chau. The brand, plus advertising under the brand, assures honest industry a market that has no limit or lurking menace. The British pioneers in brand advertising drew their inspiration from practical experience in the East Indies. They harnessed this Oriental habit to modern western inventiveness. Pears, Goodal, Backhouse & Co. and others taught British business how to advertise. They said, in effect, 'the brand's the thing, mounted on the flying horse of advertising.' It is. The brand, plus capable advertising, wins and holds the trade."

COÖPERATION WITH NEWSPAPERS A MOST POWERFUL AGENCY IN POPULARIZING FOOD AND DRUG CONTROL.

A. M. G. Soule, in an address before the twenty-seventh annual convention of the Association of Dairy, Food and Drug Officials, in Duluth last month, expressed himself as indicated by the title and he contended that it should be the duty of an official to work with representatives of the press in a co-operative way. He stated that every food and drug official will readily understand, in order to successfully enforce a food and drug law, even if the laws charged for him to en-

force are in advance of the general public knowledge, they must not be far in advance of public sentiment. Accordingly, in order to popularize food and drug control, it should be the aim of every food official to mold public sentiment to such a degree that he may have the endorsement and help of this powerful factor to assist him in his work.

MEXICO RESTRICTS IMPORTATION ON NARCOTIC DRUGS.

The importation into Mexico of all narcotics, except by the Public Health Department of the Government, has been prohibited by a Mexican decree which became effective July 28, 1923.

Responsible pharmacies legally established were previously allowed to import these narcotics after securing a permit from the Department of Health.

A FALLING OFF IN THE NUMBER OF NARCOTIC ADDICTS IN NEW YORK STATE REFORMATORY FOR WOMEN.

Superintendent Amos T. Baker of the New York State Reformatory for Women has announced that there has been a steady falling off in the number of narcotic addicts at Bedford. There are now only nine left. These are being treated by scientific methods, and the officials hope to turn them out cured.

Two years ago, when the institution first started to receive drug addicts, Bedford had sixty and the care and treatment of them was the institution's hardest problem. Reformatory officials attribute the decline in the number of women narcotic users partly to the educational and publicity campaign conducted to warn people of the danger and ravages of the narcotic habit.

BOOK NOTICES AND REVIEWS.

The Therapeutic Use of Digitalis. By G. Canby Robinson, Professor of Medicine, Vanderbilt University. Published by Williams and Wilkins Company, Baltimore. Price, $2.50.

A cardiologist recently remarked to the reviewer that probably more than half of the physicians of the United States use digitalis today with less success than Withering used it a century and a half ago, despite the fact that digitalis has been studied more intensively than any other drug with the possible exception of mercury. This fact is worth remembering when discussing a review of the subject, for it is manifestly impossible for one man to analyze every paper that has been written on the subject of digitalis and its use in cardiac disease.

The advances that have been made in the treatment of cardiac disease with digitalis, mainly within the past fifteen years, are comparable to those that have been made in the treatment of syphilis following the introduction of arsphenamine (salvarsan), or that of diabetes with the introduction of insulin. This may appear as a contradiction of the statement of the cardiologist just cited, but, in fact, it indicates the wide differences between the best methods and those which are all too common because of lack of adequate training. The treatment of cardiac disease often calls for the greatest skill, such as only the trained specialist can acquire.

Robinson wisely endeavored to select for review only those papers which have contributed to our permanent knowledge of the subject. This can be done only by one who is able and willing to analyze the studies of research workers and not merely summarize the reports of those who have attained more or less prominence in the subject under consideration, for the best men often make serious mistakes, and obscure men sometimes discover truths of the first importance (if it may be conceded that truth varies in importance).

The table of contents gives fourteen subjects and their subdivisions under which the matter is treated. The monograph embraces 137 pages with some 170 references to the literature, and since it is itself an epitome of our knowledge of the subject, it is manifestly impossible for the reviewer to give more than a glimpse of the subject in the space at his disposal.

The author devotes about ten pages to a discussion of the historical data and the different members of the group, and about as many to a consideration of the potency of these substances. It will astonish the reader to see in the table of contents that only two pages are devoted to the subject of "Animal experimentation," while some twenty pages are required for the discussion of "The toxic effects of digitalis." As a matter of fact animal experimentation is the basis for much of the review, and the reader will perceive the impossibility of separating animal experimentation from the

study of the therapeutic use of a drug of this type.

The author considers "The therapeutic effects" with reference to the actions on the heart, as shown by various changes; the effects on blood vessels, with changes in the coronary and venous circulation; and the effects on the kidneys. Following this he considers "The use of digitalis in heart failure" and "Digitalis in infectious diseases." He has not sought to give comprehensive instruction in the treatment of cardiac disease, but rather to outline the main facts and to direct the reader to sources of information; for example, he says (p. 72) "A clear understanding of auricular fibrillation is essential for the intelligent employment of digitalis. It has been especially well described by Lewis (100, 101), to whose work the reader is referred."

The pharmaceutical reader will be interested, to say the least, to find that twenty-two pages are given to the consideration of "Dosage of the digitalis bodies." Dosage constitutes one of the most difficult problems concerned with the treatment of cardiac disease, for its regulation rests upon a number of factors, including potency, absorbability, elimination, and the significance of changes induced in the heart and circulation. It is probable that no part of the monograph is more valuable than this one which is devoted to the question of dosage.

If the author does not state all that is known of the treatment of cardiac disease, he does give the intelligent reader an insight into the difficulties that attend the proper therapeutic use of digitalis, and this should lead to an appreciation of the need of the highest degree of skill when the routine administration does not cause improvement.

A reviewer is usually expected to point out the faults of a book under discussion, but the few typographical errors in this monograph will be obvious to the pharmaceutical reader, and the present reviewer knows of no others that require discussion here.

ROBERT A. HATCHER.

Traité de Matière Médicale et de Chimie Végétale, par le Dr. L. Reutter, privat-docent à l'Université de Genève. L'ouvrage formera un volume in-4 (18 x 28,5) de 850 pages à deux colonnes, avec 293 figures. Il est mis en vente en 8 fascicules de chacun 112 pages environ avec figures. Prix de chaque fascicule, 12 fr.—En vente: *Fascicules I et II*, chaque, 12 fr. (Ajouter 10% pour frais d'envoi.) (Librairie J.-Baillière et Fils, 19, rue Hautefeuille, Paris, VI.)

Parts 7 and 8 of this work complete the volume; fascicles 1–6 inclusive have had mention in preceding issues of the JOURNAL. The two parts now before us consider animal drugs according to the method followed in preceding numbers. There is an index of about 100 pages which contains not only references to the text, but also the names and very brief descriptions of drugs of not sufficient importance to warrant inclusion in the text.

A work so comprehensive can hardly fail to have its imperfections, but in looking over the pages we have failed to note any errors of consequence, even though it was, perhaps, impossible for the author to check every reference. He has given pharmacists and those who deal in drugs in a larger way a reference book of great value and usefulness, which is worthy of a place in their libraries and those of the colleges.

Rapport de la Commission de la Nomenclature Pharmaceutique. Reference to this report has been made in an editorial of this issue of the JOURNAL. The committee has performed a service of value to pharmacists and particularly for those engaged in revision work on the standards. The Federation desires cooperation and helpful criticism. There is still much work to be done on the titles of preparations which present more difficulties than the titles of drugs and chemicals from which they are prepared. The parts that have reached us are of Divisions A and B, comprising 144 pages. The work effected by the Committee deserves praise.

Rapport du Comité de la Réglementation de la Vente des Spécialités. This is another report to the International Pharmaceutical Federation and relates to the regulation of the sale of proprietary articles. The report is issued as a brochure of 24 pages. Brief reports are made by representatives from Austria, Great Britain, Belgium, France and Switzerland with an introduction by L. van Itallie and J. J. Hofman. As far as we can determine no definite action was taken on the report but the views expressed in the discussion indicate that the delegates favor that the ownership, preparation and sale of medicinal specialties should be under control of pharmacists, and only those preparations should be licensed for sale that have had the approval of competent authority. Advertising control should be in the hands of licensing authority, and the composition of the products should be declared.

A Century of the U. S. Pharmacopœia, 1820–1920. Titles, Synonyms and Abbreviations. By H. A. Langenhan, Assistant Professor of Pharmacy, The University of Wisconsin, Pharmaceutical Experiment Station.

One hundred and fifty-three pages are required for the tabulation and indicates to some extent the time and labor expended in the preparation of this bulletin. Teachers in pharmacy and students will appreciate this reference to previous Pharmacopœias not only as such but as a study of the development of the officials—the history; there is usually, if not always, reason for a change and investigation is part of research. The compiler, the University and the Pharmaceutical Experiment Station have rendered a service by the preparation of this bulletin, which may be purchased from the University of Wisconsin Pharmaceutical Experiment Station, Madison, Wis. Considering the reference work involved in the compilation the price is nominal—$2.00. It is almost a matter of impossibility to have a book of this kind free from errors; the reader is asked to advise Dr. Edward Kremers if any are found.

Eleven columns provide spaces for the editions of the Pharmacopœia; the key letters in these spaces explain the value of the title in the first column, *i. e.*, whether Latin, Official, English or Synonym, and also references to related preparations, etc., in the editions of the National Formulary. Interchanges between U. S. P. and N. F. in titles, etc., are recorded in footnotes, and changes in titles are indicated in the columns. The item ranking in the number of designations is Antimonii et Potassii Tartras (present official title): Antimony and Potassium Tartrate, Tartar Emetic (first synonym), Tartarated Antimony, Antimonyl Potassium Tartrate, Tartrate of Antimony and Potassium, Antimonii et Potassae Tartras, Tartrate of Antimony and Potassa, Antimonium Tartarizatum (first Latin title), Tartarum Emeticum, Tartarized Antimony (first English title), Emetic Tartar, Antim. et Pot. Tart. (first Official abbreviation). The only reason for noting the latter is to indicate the progress of changes and the work involved in the compilation.

CORN-MINT OIL.

Service and Regulatory Announcements, of February 14, 1923, defines corn mint, field mint, as the leaves and flowering tops of *Mentha arvensis* L.

Corn-mint oil, field-mint oil, is the volatile oil obtained from corn mint. When its normal composition is changed by partial dementholization or otherwise, it should be clearly labeled to indicate that fact.

Corn-mint oil is not recognized in the United States Pharmacopœia or National Formulary and should not be substituted for the recognized oil of peppermint, derived from *Mentha piperita,* in pharmacopœial and formulary preparations without appropriate label declaration. Foods, beverages, and confections flavored with corn-mint oil should not be designated by such unmodified terms as "mint" or "mint flavored."

Shipments of corn-mint oil offered for import will be permitted entry if the product is properly invoiced, labeled, and sold, and when proper information is given as to its ultimate use, in accordance with the usual requirement made for substitutes, outlined in item 275, page 96, *Service and Regulatory Announcements,* Chemistry 23.

Manias and Mind Medication, an address by John Uri Lloyd, reprint from *Eclectic Medical Journal,* March, April, May and June 1923.

Animal-Eating Plants, one of a series of popular lectures given at the Philadelphia College of Pharmacy and Science, by Heber W. Youngken. Reprint from *American Journal of Pharmacy,* June 1923.

New Sources of Santonin, by Arno Viehoever and Ruth G. Capen. Contribution from Pharmacognosy Laboratory, Bureau of Chemistry. Reprint from *Journal of the American Chemical Society,* August 1923.

Bulletin A5 of Drug Trade Bureau of Public Information relates to Plant Science Seminar at the University of Minnesota. Director Robert P. Fischelis, 509 High St., Newark, N. J., would be pleased to have clippings from newspapers publishing all or part of the bulletin.

NEW PUBLICATIONS.

Analysis: Traité d'Analyses des Substances Minérales Metaux. By Adolphe Carnot. Revised and enlarged with appendix by E. Goutal. 1050 pp. Price, 65 fr. Dunod, Paris.

Oils: Examination of Hydrocarbon Oils and Saponifiable Fats and Waxes. By D. Holde and Edward Mueller. 2nd edition. 572 pp. Price, $6.00. John Wiley & Sons, Inc., New York.

'Ler Produits Chimiques purs en Photographie: Leue nécessité; Leur emploi: leur contrôle.—Par Camille Poulenc. Docteur ès Sciences Pp. 160. Pr., 2 fr. 50. Paris: Charles Mendel, 118, rue d'Assas.